ROLE OF VITAMIN-A
IN CERTAIN SKIN DISEASES

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C O N T E N T S

I N T R O D U C T I O N

The conception of deficiency diseases, particularly of the nutritional group is quite new. The discovery of the vitamins has opened a wide field in medical research. Gradual realization that many human diseases were not produced by infections or toxins but by vitamin deficiencies led to the conception of various deficiency diseases. Until recently the vitamins were only of clinical interest in the treatment of certain types of deficiency diseases but it is now realized that in large doses vitamins can be used in other conditions therapeutically.

The next stage in the history of vitamin research consisted of distinguishing individual vitamins, their isolation, analysis and synthesis.

Vitamins A and D apparently exist only in the bodies of vertebrates. Vitamin A can, however, be formed in the mammalian body from certain red and yellow pigments, carotenoids, which are to be found in many plants, micro organisms and vertebrates. Such substances are termed "provitamins".

FUNCTIONS OF VITAMIN - A

By no means do all animals require all the vitamins. While the water-soluble vitamins appear to form an essential part of bio-chemical machinery of almost all cells, vitamin A and D are apparently needed only by vertebrates.

Vitamin A is essential to growth, vision and to the integrity of the epithelial tissues (McLester, 1949).

GROWTH: Vitamin A has specific effect on the growth of animals (Patterson, 1942) and accelerates the growth and the life of tissue cultures (Baker, 1935; Batchelder, 1934). There is no definite information concerning the function of vitamin A in the metabolic processes of the body. The requirement of the body for vitamin A depends upon the weight and not on metabolic activity. In rats on a Vitamin A deficient diet the skeleton probably ceases to grow before any of the other tissues of the body, which suggests that vitamin A has a specific influence on the growth of bone (Wolbach and Bessey, 1941). The morphology of the bones of young rats, however, is not greatly altered in striking contrast to that of puppies or calves. It would seem, therefore, that while vitamin A has a profound effect on the growth of bone, this effect varies in different species.

Since young rats do not gain in weight with vitamin A deficient diet it was thought at first that vitamin A has a specific growth promoting effect. It has been shown, however, that skeletal growth continues though the animals fail to gain in weight.

VISION: Vitamin A is concerned in vision. In the retina it unites with a protein to form the visual purple. Vitamin A is essential for vision in dim light. Night blindness occurs in man and animals as a result of vitamin A deficiency.

In bright light vision is carried out by the cones of the retina, which probably are not affected by lack of vitamin A, though this is not certain (Lythgoe, 1940; Wald and Steven, 1939). In dim light lack of vitamin A generally decreases the sensitivity of the cones. Cones are used in bright light and the rods in poor light. The rods, however, are not directly stimulated by light, but only indirectly through the chemical changes light causes visual purple. Visual purple is a complex substance of which vitamin A is a component. Since vitamin A must slow down the formation of visual purple and so slow down dark adaptation. Measuring this dark adaptation has been used to ascertain the vitamin A nutrition of a subject.

Night blindness is due to failure in regeneration of the visual purple after the eyes have been exposed to bright light.

For centuries poorly fed fishermen have known that a single day's exposure to glare from the water often causes sudden night blindness. The Ebers Papyres, written about 1600 B.C., probably referred to night blindness when liver was recommended for the eyes, while the Chinese in 1500 B.C. were giving liver and honey for night blindness. One of the oldest physicians of India was using liver therapy orally and as compress locally on the eyes as far back as 200 B.C. Hippocrates advised the whole liver of an ox dipped in honey and liver was known to later Roman writers. Guillemean in France in the 16th century besides clearly describing night blindness, advised liver for its cure. Drummond and Wilbraham (1939) find that the first mention of liver for the eyes in England was in Muffett's "Health Improvement" of 1655.

It has later been found out by some workers in the line that vitamin A deficiency is not the only cause of night blindness, and even when it is the cause the visual defect cannot always be attributed to failure in the regeneration of visual purple, for degenerative changes in the visual receptors or of the neural elements of the retina may be a /

relatively early effect (Best and Taylor, 1945).

EPITHELIAL TISSUE: The Keratinization of the epithelial tissues of the body and of the skin in particular is controlled by vitamin A.

Changes in the skin and poor dark adaptation are the earliest signs of a definite deficiency which can be diagnosed. Both in Africa and India skin changes due to lack of vitamin A were present in 80 per cent of some groups of children (Loewenthal, 1935; Nicholls, 1935).

Vitamin A is necessary for some particular metabolic process peculiar to all epithelial cells in varying degrees but not to other tissues (Masson, 1933).

The most significant function of vitamin A is its influence in maintaining the structural intigrity of epithelial cells.

CHEMISTRY OF VITAMIN - A.

Karrer and his co-workers (1930) in Switzerland first suggested the formula for vitamin A to be $C_{20}H_{29}OH$. Heilborn and his associates (1932) in England and Euler (1932) in Germany confirmed this chemistry of vitamin A. Karrer (1936) further experimentally established that vitamin A is produced within the body from one of its carotenoid provitamins.

It has recently been shown that alpha particle bombardment with radon also effects the conversion of Kitol to vitamin A (Libermann and Grundland, 1947).

Kuhn and Morris (1937) synthesized vitamin A though it could not be obtained in pure form. Holmes and Corbett (1937) in the same year isolated which appeared to be the pure vitamin A.

Crystals of vitamin A are pale yellow in colour, M.P. 5.5 to 6°C, viscous oil at room temperature. Munsell (1938) has assayed the substance by a biological method and also with the Carr-Price method. Morton and Heibron (1938) and Hume and Chick (1935) examined the absorption in the ultra-violet light. Sobotka and his associates (1943 and 1944) showed that vitamin A exhibits fluorescence when irradiated by a mercury vapour lamp. This/

This fluorescent property has been used by Popper (1944) to demonstrate vitamin A in tissues. Morton and his coworkers (1948) have developed a method for the preparation of vitamin A - aldeyhyde.

Biological activity is lost when it is reacted on by some chemicals but in the absence of oxygen it can resist very high temperature such as 120°C. When oxygen is present it is slowly destroyed even at room temperature (Drummond and Coward, 1920; Lilva, 1920).

Many fats when heated develop an "anti - vitamin A" factor which destroys the biological activity of vitamin A. It is not yet known whether this is a chemical or a biological effect (Beck and Peacock, 1941; Dyne et al, 1941).

Vitamin A and its carotenoid precursors are fat soluble. Separation of vitamin A from carotenoids can be carried out by dissolving both in petroleum ether and adding alcohol, when the latter will dissolve the vitamin A but not the carotenoids. Since alcohol and petroleum ether are not miscible, the alcohol layer containing the vitamin A can be separated easily.

The colour reaction of vitamin A are of great practical importance. Rosenheim and Drummond (1920) found a typical colour reaction with sulphuric acid and vitamin A. Vitamin A gives a colouration with chlorides of polyvalent metals /

(Rosenheim and Drummond, 1925). Carr and Price (1926) have found the antimony trichloride as the most satisfactory reagent and this colour reaction being extensively used for the assay of vitamin A nutrition. With vitamin A a blue colour is developed in antimony trichloride and this is called the blue colour reaction. The other method is the development of pink colour by the action of vitamin A and activated glycerol dichlorhydrin and this is called the pink colour reaction (Sobel and Rosenberg, 1948). Higher vitamin A values have been obtained in blood by using Sobel-Werbin reagent than by Carr-Price reagent (Sobel and Snow, 1947). This reagent does not give any colour with the carotenoids whereas Carr-Price reagent gives colour reaction with carotenoids.

SOURCES OF VITAMIN - A

The main source of vitamin A are the provitamins or carotenoids. Hence it is essential to consider such provitamin A also.

PROVITAMIN - A: The precursors of vitamin A are synthesized by plants and these substances are known as carotenoids. Vitamin A in the form of its precursor, the yellow pigment carotene, is widespread in nature, being formed chiefly in association with chlorophyll in the green leaves of plants. This biological relationship of these two pigments is not known (McLester, 1949). The exact role of carotene in the plant economy is not known. The carotenoids appear when growth is active and suggestive parallelism has been noted between carbon dioxide assimilation through chlorophyll and carotenoid concentration.

Carotene is widely distributed in nature being found both in bacteria (Karrer and Solmssen, 1936) and also in the higher plants. In plant tissues there is a definite relationship between their green or yellow colouring and their vitamin A activity. Vitamin A is found in the body from certain of the red or yellow plant pigments known as carotenoids. No animal can apparently make carotenoids (Morton, 1940). Carotene is present/

in animal tissues and particularly in corpus luteum and suprarenal glands (Mason, 1933). Of the many corotenoids, only alpha, beta, gamma and xanthene are known as "provitamin A".

VITAMIN - A: Harbivorous animals depend entirely on corotene for their vitamin A but no animal can apparently make corotenoids for themselves, nor for vitamin A from any other sources (Morton, 1940).

The chief sources of vitamin A are mammalian and fish, egg, milk and milk products and various types of oils like cod liver oil, red palm oil, pea-nut oil and some of the cereals. Omnivorous animals like human beings obtain vitamin A partly from corotene and partly from animal foods in which the vitamin A itself is present. How fish acquire large stores of vitamin A in their livers is not known (Edisbury et al, 1938).

ABSORPTION OF VITAMIN - A

PROVITAMIN - A: Since corotene is very slowly absorbed the body tends to be wasteful of corotene. Wald and his associates (1941) have experimentally found that after corotene is consumed absorption from the intestine continues for 2 or 3 days and excretion in the faeces continues for a week. In man, reports differ as/

to the amount of carotene absorbed from various foods. Wilson (1937) found that 80 to 90 per cent of the carotene in spinach is absorbed when added to a normal diet. Kreula and Vitrneu (1940) have reported that only 20 per cent of the carotene of raw carrots and 5 per cent of the carrots cooked are absorbed. Graves (1942) has found only 1 per cent of carotene absorbed when raw carrot is consumed and 19 per cent when cooked. Clausen (1943) has observed poor absorption of carotene from raw vegetables and found rapid absorption from solution of digestible oils.

VITAMIN - A: The absorption of vitamin A by the lymph stream has been demonstrated in several species of animals and even in human subjects (Drummond et al, 1935), in dogs (McCoord et al, 1943), in rats (Popper and Volk, 1944; Radice and Harraiz, 1947), and in sheep (Eden and Sellers, 1949).

Further studies on the mechanism of vitamin A absorption have been made by Gray and his co-workers (1940). They have shown that vitamin A esters are hydrolysed in the intestinal tract of the rat. Eden and Sellers (1950) have experimentally determined in adult sheep and calves by dosing with vitamin A and finding the vitamin A - alcohol and/

ester in the intestinal content, mucosa, lymph and blood and concluded that after passing across the intestinal wall the absorption of vitamin A apparently remained esterified, as the rise in the vitamin A content of the intestinal lymph following administration of either form was nearly all in the ester fraction. In the normal adult blood also the increase after administration of vitamin A was mainly in the ester form as found out by micro method using aluminium oxide as absorbent for separating vitamin A - alcohol from the esterified form.

ROUT OF ABSORPTION OF VITAMIN - A: Using different routs of administration absorption of vitamin A has been studied by various workers. Wald and his associates (1941) have observed rapid and complete absorption of vitamin A when administered by mouth.

Clausen (1943) has observed that during absorption vitamin A is promptly re-esterified and enters the portal vein and thoracic duct.

TIME FOR ABSORPTION: Various workers have attempted to determine the time for the absorption of vitamin A by estimating blood vitamin A concentration. Clausen and McCoord (1938) have found the maximum rise in the level of vitamin A in the blood occuring within 3 to 5 hours of its being taken by mouth. While Ruch and his associates (1946) carried on investigations in a large number/

of normal human subjects and found the maximum absorption at the sixth hour after oral administration. This experiment has been named as the "Vitamin A tolerance test". But "Vitamin A clearance test" is more comprehensive and has been suggested by Stewart (1950).

STORAGE OF VITAMIN - A

PROVITAMIN - A: Carotene undergoes no change during intestinal absorption since it is active when given by innuction through the skin (Eddy, 1939) or injected into the tissues though much is destroyed at the site of injection (Wald et al, 1941). After injecting carotene into the circulation it can be detected stored in the Kupffer cells (Lasch, 1935) from where it gradually disappears.

CONVERSION OF CAROTENE TO VITAMIN - A: Since the recognition that carotene is the precursor of vitamin A, problems of where and how it is converted into vitamin A in the animal body have been discussed. Moore (1929) first observed that since on feeding vitamin A depleted rats with carotene vitamin A appears in the liver. Jansen and With (1939) experimentally confirmed that conversion of carotenoids into vitamin A takes place in the liver. The conversion of precursors into vitamin A takes place in the liver has been recognised fully. The/

The change of carotene to vitamin A has been observed by incubating carotene with fresh liver tissue experimentally (Olcott and McCann, 1931). Repeating the same experiment with liver which has been previously heated they could not get any conversion of carotene to vitamin A.

Some recent works, however, indicate that the intestinal wall and not the liver is the most likely site in which this conversion from carotene to vitamin A takes place (Mattson et al, 1947). To confirm the result further work has been done by Wiese and his associates (1947) who studied in vitro the transformation of carotene to vitamin A by the small intestine and confirmed the results of Mattson and his co-workers (1947). During this time a band of workers concluded after extensive experimental work that evidence in support of the theory that liver was the site of conversion of carotene to vitamin A was unsatisfactory (Malison et al, 1947) and found evidence that conversion occurred in the intestinal wall. Further work for the conversion of carotene to vitamin A has been done by Krause and Pierce (1948) to determine whether liver is necessary and they concluded that hepatic circulation is not necessary for conversion.

Thomson and his co-workers (1949) have experimentally found vitamin A within 15 minutes of dosing in the intestine after carotene meal and in/

the lymph appeared 1 to 2 hours after but none appeared in the blood or in the liver. They concluded that vitamin A arising from carotene in the intestine is carried thence by the lymph to the blood and by the blood to the liver. Later on Thomson and his associates (1950) have further experimentally shown that carotene is converted into vitamin A in the small intestine of the rat, pig and chick.

VITAMIN - A: Vitamin A is stored in the liver. In well nourished persons, about one-tenth to one-fifth of the total vitamin A is present as the provitamin A. Carotene is stored in the liver and body-fat. In man 70 to 95 per cent of the total amount in the body is stored in the liver. Once stored in the liver, vitamin A disappears slowly, but excessive amounts disappear rapidly. The ability of the liver to store vitamin A is decreased in hepatic cirrhosis and in chronic nephritis. Fevers not only interfere with absorption of vitamin A but increase its rate of disappearance from all tissues. It disappears most rapidly from the blood and least rapidly from the liver (Clausen, 1943). Davies and Moore (1934) have shown experimentally that with moderate stores in the liver small amounts of vitamin A were always present in the kidneys and sometimes in the lungs. They further observed that the suprarenal glands /

also, but inconstantly, stored vitamin A in large amounts, while all the other tissues of the body contained traces of vitamin A. Other workers have observed in human beings that the adrenals, testes and ovaries - from infancy to the climacteric - and the lactating breast are all said to store vitamin A (Ragins and Popper, 1942).

The normal storage in human adults from the ages of fifteen to fifty nine is given by Moore (1937) as being 220 international units per gram of the wet liver; other workers report higher values (Ralli et al, 1941; Haig and Patek, 1942). Moore (1937) has found in healthy children the average of 130 I.U. of vitamin A in the liver. Popper (1944) has also found very low store of liver-vitamin A in young infants per gram. In five month's embryo the stores of vitamin A are reported to be high (Popper, 1944). In the young of animals the reserves of the suckling vary with the maternal diet (Dann, 1932) and since pregnant women are often deficient in vitamin A (Cowell, 1940) the low reserves of the infants are probably in part explained by their mother's diet.

The essential unsaturated fatty acids interfere with the vitamin E absorption and thus hampers the storage of bitamin A (Sherman, 1941).

VITAMIN - A DEFICIENCY

Vitamin A deficiency may be due to

(1) Lack of vitamin A in diet

(2) Inefficient absorption of vitamin A

(3) Excessive destruction of vitamin A in the body

(4) Failure of utilization of vitamin A in the body

(5) Other factors such as: (A) Intestinal integrity.
(B) Defective storage in liver.
(C) Liver disease.
(D) Influence of other vitamins.
(E) Influence of endocrine glands.
(F) Influence of Chöline.

(1) LACK OF VITAMIN - A IN DIET: Deficient or unbalanced diet, inadequate dietary intake and bad dietary habits are responsible for deficiency in vitamin A intake. Even nutritional failure should not be underestimated, in view of the attention which vegetables must receive if a dietary sufficiency is to be obtained as the habit of sufficient amount of vegetables varies greatly among individuals. Brown and Morgan (1948) report that vitamin A is essential for the growth of tissue protein but not for its maintenance. Children especially need vitamin A itself, as their utilization of carotene is poor (Nicholls and Nimalasuria, 1941). Pregnancy and lactation, which are common causes of a deficiency of vitamin A in all countries, increase the maternal need for vitamin A.

Protein diet itself is a source of Vitamin/

intake whereas high carbohydrate diet increases the demand for vitamin.

Some subjects although presenting a semblance of health, live in the "twilight zone of nutrition" with no factor of safety and when pregnancy or illness supervenes an overt deficiency syndrome is made apparent (McLester, 1943).

Shafar (1949) thinks that in general, nutritional deficiency may originate either in the secondary or conditioned form, in which there is some other abnormal condition responsible for precipitating the malnutrition. Conditioned malnutrition is produced by interference with ingestion, absorption or utilization. Malnutrition factors with definite relationship with vitamin deficiencies have been established by various workers (Jollifee and Smith, 1943).

(2) INEFFICIENT ABSORPTION OF VITAMIN - A.

PROVITAMIN - A: Vitamin A defects may be due to inefficient absorption of provitamin A from the intestinal tract. Wilson (1937) reports that in man on a fat free diet the absorption of provitamin A is nearly halved. Heymann (1936) attributed the poor absorption of provitamin A during toxic fevers to the poor absorption of fat, which is further borne out by his finding no absorption in a child with caeliac disease. Bile is necessary for the/

absorption of provitamin A. When the normal amount of bile is not available due to disease or obstruction provitamin A absorption is greatly reduced. Liquid paraffin interferes with the absorption of provitamin A from the intestine. Deficiency of vitamin E intake is responsible for lack of absorption of provitamin A. Infectious diseases greatly hamper provitamin A absorption from the gut.

VITAMIN - A: Absorption of vitamin A and provitamin A are better when administered orally than when administered by injection (Freedman, 1948; Sullman, 1948). Age interferes with the absorption of vitamin A (Rafsky and Newman, 1948). Mahle and Patton (1947) have observed that mineral oil and hydrophilic mucilloid laxatives reduce the absorption and availability of minimal amounts of vitamin A. Parasites in the small intestine may adversely affect the metabolism of vitamin A (Sandels et al, 1941).

Liver has an extremely high power of absorbing vitamin A (Moore, 1946).

(3) EXCESSIVE DESTRUCTION.

Vitamin A deficiency may result from excessive destruction of the vitamin. Anti-oxidant is necessary before absorption, during absorption and/

also in storage of vitamin A and provitamin A. Vitamin E is the anti-oxidant substance which is essential to prevent destruction of vitamin A and provitamin A. Only vitamin E cannot check destruction of vitamin A but ethanolamine and ascorbic acid are recommended for the preservation of vitamin A (Kren and Autosh Kiev, 1948). Vitamin A and E are readily destroyed by oxidation. Oxidation rancidity of fats included in the diet may destroy these vitamins with the consequent deprivation (Mattill, 1938; Whipple, 1936).

Vitamin A is destroyed to a great extent in the mouth by saliva and again in the stomach by the gastric juice. Layman and Kuiken (1948) have experimentally found that the saliva and gastric juice of babies from birth to four years of age, when incubated with vitamin A, destroyed up to 65 per cent of the vitamin, with the greatest amount of destruction occuring within the first five minutes.

When the necessary amount of vitamin E is not present in the diet and is destroyed previous to absorption and if there is deficiency of vitamin E in the liver vitamin A storage is deficient and undergoes destruction in the liver.

Estrogen present in the liver destroys vitamin A when other vitamins are lacking (Singher et al, 1944). /

There is destruction of vitamin A in various infectious diseases.

. Some amount of vitamin A is destroyed in the oily vehicle it is supplied.

(4) FAILURE OF UTILISATION.

Vitamin A deficiency may result from failure of utilisation of provitamin A and vitamin A.

General metabolic failure may be responsible for the defective absorption of vitamin A. This may result in a faulty utilisation of absorbed vitamins but Frazer (1949) thinks it is difficult to establish vitamin deficiency in such a condition. Faulty utilisation of vitamin A has been described in cases of alcoholic cirrhosis (Patek and Haig, 1939).

Failure of utilisation of vitamin A can be influenced by factors influencing absorption of the vitamin. Fat in normal amounts aids absorption of vitamin A and in all diseases where the absorption of fat is impaired the absorption of vitamin A is also impaired though decreased intestinal motility also play a part, since cascara and prostigmin increases absorption of the vitamin in fibrocystic disease of the pancreas (Flax et al, 1942) while in normal subjects atropine decreases it (Ingelfinger et al, 1943). When there is some other abnormal condition responsible for /

precipitating the malnutrition this state is called conditioned malnutrition. Conditioned manutrition is produced by interference with utilisation of vitamins besides other factors (Shafar, 1949).

In certain diseases the utilisation of vitamin A by the body is impaired.

Certain animals as the cat cannot utilise carotene. Children utilise carotene badly (Nicholls and Nimalasuria, 1941).

Sherman (1947) has observed that utilisation of both vitamin A and provitamin A is influenced by the vitamin E content of the diet.

(5) OTHER FACTORS RESPONSIBLE FOR VITAMIN - A DEFICIENCY.

Vitamin A deficiency may be due to various other factors such as:

(A) INTESTINAL INTEGRITY: Intestinal integrity is important for proper absorption of provitamin A and vitamin A from the intestinal tract and also for conversion of provitamin A to vitamin A. Striking changes are found in the intestine due to lack of vitamin A. The outstanding histological feature is the tendency for the columner epithelia to be transformed into stratified epithelia which may hamper the absorption of vitamin A and provitamin A from the gut. Since it has been shown recently that provitamin A is converted into vitamin A in/

the wall of the intestine it is likely that this process of conversion may be interfered with in the wall of the intestine which has undergone stratified changes in the epithelia and where the mucous secreting cells of the intestine are atrophied and the tips of the villi are necrosed with masses of bacteria filling the lumina of the gland all these as a result of avitaminosis A. Vitamin A is essential for the maintenance of the epithelial integrity (Anderson et al, 1950).

Vitamin A absorption may be upset due to intestinal deficiency. Frazer (1949) believes that signs and symptoms of vitamin deprivation may occur even though the diet contains adequate amounts of vitamins and in the absence of any evidence of destruction in the food. This may be due to faulty digestion of the vitamins, or their inclusion in unabsorbed residue.

(B) LIVER: The amount of vitamin A in the liver of humans is usually a reasonable indication of the vitamin A status of the body. An exception is acute liver disease, in which case the amount of vitamin A in the liver can be quite normal or even above normal, and still the individual may suffer from vitamin A deficiency because of the inability to utilise vitamin A from storage (Harris, 1949). Liver concentration of vitamin A in normal human subjects have been reported by various workers/

from different countries such as from Africa 800 international units per gram by Auffret and Tanguy (1948), from Egypt 130 international units per gram by Nor-El-Din (1944), from England 300 international units by Harris and Moore (1947) and from Scotland 500 international units per gram of liver by Dzialoszynski and Tomaszewski (1947). Normal human reserve of vitamin A would be 400 international units (Moore, 1946).

The role played by the liver in nutritional deficiencies has been recognized by many workers experimentally and it has been concluded that the normal liver function is in part dependent on optimal nutrition. Proteins, phospholipids and vitamins have been observed in human portal cirrhosis and the conception of this disease complex has undergone many changes as a result.

(C) LIVER DISEASES: Diseases of the liver act as a contributory factor in nutritional disorders. The high content of nicotinic acid - containing enzymes in the liver and the depletion of these enzymes in the livers of nicotine acid - deficient dogs point to the probability that other "vitenzymes" are stored in the liver. The author observed a much quicker improvement in the function of the liver with vitamin A and vitamin C than with vitamin C alone (Lahiri, 1943).

(D) OTHER VITAMINS: There are indications that/

this synergistic action of vitamins has considerable clinical importance. Vilter and his co-workers (1939) have demonstrated the effect of riboflavin on the symptoms of pollagra in relapse. Smith and Martin (1940) have found response in perleche and cheilosis to pyridoxine after riboflavin failed to cure this may also be interpreted as a co-vitamin effect. Kimble and Gordon (1939) have shown that riboflavin, or in some cases vitamin C, rapidly raised the vitamin A content in the blood to the normal level, where prolonged vitamin A dosage was unable to do so. Hickman and his associates (1944) believe that one significant chemical property of vitamin E is its anti-oxidant activity and they concluded that this could be used, for example, for the protection in the alimentary tract or in the cells of vitamin A and carotene, both of which are peculiarly susceptible to oxidation. Because of this factor of vitamin E it is possible for an animal, supplied liberally with this factor, to subsist and accumulate reserves of vitamin A upon a diet which otherwise would be difficult in this respect. Vitamin E is responsible also for the storage of vitamin A in the liver. Moore and Davies (1941) have suggested that vitamin E spares hepatic stores of vitamin A and that it protects it against oxidation within the liver. There is an optimal/

ratio between the vitamins A and E in the diet which has been noticed by various workers (Moore, 1940). Vitamin E is most effective when fed together with vitamin A; the effect of injected vitamin A is enhanced by oral vitamin E. In man vitamin E does not affect the vitamin A tolerance curve (Steigmann and Popper, 1944).

Other vitamins also assist indirectly in the absorption of vitamin A. There seems to be some relationship between vitamin B deficiency and absorption of vitamin A. It is stated that vitamin A deficient rats cannot utilize vitamin C given by mouth. Boyer et al (1942) state that the urinary secretion of vitamin C in the rat is greatly reduced by lack of vitamin A, while Mitolo (1942) reports that in scurvy the amount of vitamin A in the livers of guinea-pigs goes down. Scorbutic symptoms in vitamin A deficient rats has been observed (Mayer and Wrehl, 1948). Mapson and Walker (1948) however have found no relationship between vitamin A and C.

(E) ENDOCRINE INFLUENCE: Hypo or hyper function of ductless glands results in deficiency of vitamin A nutrition. Inter relationships between the metabolism of vitamin A and the function of various hormones are still controversial. Sadhu (1948) and Couceiro et al (1947) have found experimentally that vitamin A is antagonistic to/

the thyrotropic hormone. Thyroid hormone stimulates the conversion of carotene to vitamin A (Popper, 1941) and vitamin A decreases the effect of thyroxin as a stimulant of metabolism. Robinwitz (1931) claimed that vitamin A increased iodine activity in hyperthyroidism. This view point has been supported by Fraser and Cameron (1931) and Abelin (1936) reported that animals given thyroid had an increased requirement for vitamin A. In man the importance of the thyroid for converting carotene to vitamin A is shown by the occurrence of night blindness in hypothyroidism and by the low level of vitamin A (Wahl, 1939). The inter relations between thyroid function and vitamin metabolism has been studied most fully by Drill (1943). It is now certain that; (a) the thyroid stimulates the conversion of carotene to vitamin A but does not increase the body's requirements of the latter, (b) vitamin A increases the thyroxine in stimulating metabolism.

Kepinov (1939) in some very interesting experiments on starved frogs found that adrenaline did not accelerate the hydrolysis of liver glycogen to glucose unless vitamin A was previously given. Davies and Moore (1934) and Popper (1940) and again Popper (1941) believe that the adrenals take part in the storage of vitamin A and their function may possibly be affected by vitamin A deficiency. /

Johnson and Baumann (1947) have observed that the concentration of vitamin A in the kidneys is usually high. This has been confirmed by Eden and Moore (1950).

Vitamin A apparently stimulates the glycogenic hormone of the pituitary (Kepinov , 1939). The principle of the pituitary which stimulates lactation does not appear to be affected by vitamin A since Williams and his co-workers (1940) found that the amount of milk secreted by nursing mothers was not altered by varying their intake of vitamin A. Whether vitamin A in its action on oestrus and pregnancy acts directly on the ovaries or through the pituitary is not known. Mason and Ellison (1935) observed that in rats oestrus is not stopped by a deficiency but becomes delayed and irregular. Sherwood and his associates (1936) have observed in rats to stop oestrus and a desire to mate with excessive amounts of vitamin A. Truscott (1947) reports a direct action of vitamin A on the growth and development of the ovary which would undoubtedly be reflected in its function. Continued cornification of vaginal epithelium is considered to be a reliable early manifestation of vitamin A deficiency in female rats (Aberle, 1936). Sherwood and his co-workers (1937) and Thorborg (1948) reported that feeding large amounts of provitamin A suppressed the oestrus vaginal smear picture in the /

normal rat; however other workers administered orally (Burill and Green, 1941) or by injection (Brody and Goldman, 1941) and found no inhibition of the vaginal response. Recent studies on mice tend to corroborate the observations of Sherwood and his associates (1937) and has been experimentally proved by Thorborg (1948). Singher and his co-workers (1944) made studies bearing on the relationship of Vitamin A deficiency to the capacity of the liver to inactivate oestrogms and found the loss of inactivating ability paralleled the decrease of vitamins in the liver. Cantrew and his associates (1943) corroborated experimentally the inactivating power of liver of oestrogm. Perlman (1948) believes that nutritional factors must be considered with in evaluating the level of oestrogen metabolism in the oestrgen. Longwell and McKee (1942) pointed out that liver appears to be intimately linked with the metabolism of oestrogm.

Androgen may possibly serve as precursors of oestrogenswith organisms (Butenandt and Kidszus, 1935) and evidence has been obtained which indicates that ovaries secrete androgenic substances (Pincus and Perlman, 1943). During the first six years of life, boys show an extremely low level of androgenic material in the urine but the rate of increase in the urinary excretion of androgenic material continues to rise up to about eighteen/

normal rat; however other workers administered orally (Burill and Green, 1941) or by injection (Brody and Goldman, 1941) and found no inhibition of the vaginal response. Recent studies on mice tend to corroborate the observations of Sherwood and his associates (1937) and has been experimentally proved by Thorborg (1948). Singher and his co-workers (1944) made studies bearing on the relationship of Vitamin A deficiency to the capacity of the liver to inactivate oestrogms and found the loss of inactivating ability paralleled the decrease of vitamins in the liver. Cantrew and his associates (1943) corroborated experimentally the inactivating power of liver of oestrogm. Perlman (1948) believes that nutritional factors must be considered with in evaluating the level of oestrogen metabolism in the oestrgen. Longwell and McKee (1942) pointed out that liver appears to be intimately linked with the metabolism of oestrogm.

Androgen may possibly serve as precursors of oestrogenswith organisms (Butenandt and Kidszus, 1935) and evidence has been obtained which indicates that ovaries secrete androgenic substances (Pincus and Perlman, 1943). During the first six years of life, boys show an extremely low level of androgenic material in the urine but the rate of increase in the urinary excretion of androgenic material continues to rise up to about eighteen/

years of life. The increasing concentration of androgns and 17-ketosteroids in urine with increasing age in girls presents a picture similar to that found in boys. The urinary levels attained by both boys and girls are quite similar. Ovary does in fact contribute andrgens (Dorfman, 1948).

(F) INFLUENCE OF CHOLINE: Choline is essential for storage of vitamin A. Popper (1944) reports that in rats on a diet deficient in choline with ample carotene no vitamin A is stored in the lupatic or kupffer cells, though it is present in abnormally large amounts in the kidney. When vitamin A itself is given in the diet the kupffer cells but not the hepatic cells contain vitamin A. Other workers have thought that a deficiency of choline may hasten the depletion of hepatic stores of vitamin A (Clayton and Baumann, 1944).

EXPERIMENTAL VITAMIN-A DEFICIENCY IN HUMAN SUBJECTS

It is very difficult to obtain volunteers to experiment with vitamin A deficiency.

However, Steffens and his associates (1939) carried on experiments on human subjects on a vitamin A deficient diet and found experimentally /

that these subjects developed follicular hyperkratosis after 190 days.

Mann (1926) experimentally has shown that boys of 7 to 11 years of age on basic diet with restricted amount of vitamin A developed roughness of the skin, amounting in some cases to minor degrees of ichthyosis. Block (1921) observed dry skin in children suffering from avitaminosis signs. At this age deficiency of vitamin A is associated with general dryness of the skin and follicular keratosis has been observed by Frazier and his co-workers (1943).

The specific tissue changes due to deprivation of fat soluble vitamin A is replacement of various epithelia by stratified squamous kratinizing epithelium. This is true for all tissues of the body of epithelial origin. The change in the epithelium is the same in all areas where it occurs, the epithelium becoming undermined by stratified epithelium, which starts to be formed by the basal layer of cells in many places at the time. The basal cells themselves, however, are not changed, maintaining their individual properties, so that when vitamin A is given to a deficient animal the basal cells promptly start to replace the stratified epithelium of the correct type (Bicknell and Prescott, 1948).

RELATIONSHIP OF VITAMIN-A DEFICIENCY AND CERTAIN SKIN DISEASES

Far-reaching advances have been made in the field of nutrition during the past two decades. More and more diseases are being associated with dietary deficiencies, especially with inadequate supplies of certain vitamins.

Urbach and Le Winn (1946) observed that "It was the discovery and the demonstration of their clinical deficiency that really brought nutritional therapy into its own in certain skin diseases. Diseases such as pillagra, phrynodroma, keratosis follicularis, Pityriasis rubra pilaris tropical ulcer and others, which were regarded as hopeless or at least intractable, only ten years ago, can now be cured in a few months".

The rapid developments of recent years in the field of nutrition have had their influence on dermatologie thinking as well as on therapy.

The well-recognised fact that a deficiency of nicotinic acid can produce characteristic lesions of the skin and mucous membranes in itself signifies that cutaneous errutions can develop as a result of cellular disturbances which have their origin in nutrition. Biochemists have recognised that these cellular disturbances are due to an interference with the process of biologic oxidation and other enzyme enzymatic functions, which fits in well with the/

concepts first expressed by the founder of modern histopathology of the skin, Unna (Gross, 1944).

While during nutritional survey in Nigeria Nicol (1949) observed various skin diseases due to vitamin A deficient diet which were mainly of two varieties: (1) Follic ulosis (keratosis pilaris) - a simple enlargement or undue prominence of hair follicles, without obvious hyperkeratosis which may be on either a healthy-looking or a xerotic skin, (2) follicular hyperkeratosis (Phrynoderma) marked thickening of hair follicles with projecting primary plugs of keratinized material, occuring superimposed upon a generalized xerosis and seems to be related to avitaminosis A.

The relation of this sign to avitaminosis A has been detected in recent years.

Different workers from all over the world are reporting cases of avitaminosis A and also good response to many skin diseases with vitamin A therapy.

Youmans (1943) observed that deficiency of vitamin A not only causes night blindness, xerosis and xerophthalmia but also causes specific dermatosis and changes in the epithelium of certain internal organs, and a mild, latent, or subclinical deficiency may exist, presenting not clearly recognizable clinical signs or symptoms but detectable by instrumental means.

From/

From the literature available on vitamin A in relation to skin diseases the diseases can be grouped as follows: (1) where vitamin A deficiency is responsible for the causation of the lesion, namely Ichthyosis, phrynoderma, Darier's disease, pityriasis rubra pilaris and pigmentation, (2) Where observers have claimed relationship of the diseases with avitaminosis A such as acne vulgaris, nummular eczema, brittleness of the nail, alopesia, callous and canitis and various other skin diseases, (3) Where vitamin A nutrition has been observed to be higher than normal, (4) correlation with vitamin A and androgen in certain skin diseases.

DIFFERENT SKIN CHANGES IN AVITAMINOSIS-A.

(1) ICHTHYOSIS: When dryness of the skin is present it is called xerodermia. With dryness of the skin there may be associated phrynoderma due to vitamin A deficiency and has been noted by a large number of workers in the Eastern countries. With the dry skin there may be pigmentation of the skin like melanosis due to vitamin A deficiency. When the vitamin A deficiency is very chronic and of severe nature the dryness may increase further and fish-scale condition of the skin results which is called ichthyosis. It is not an uncommon condition in the East and has been reported by a host of /

workers.

Frazier and Hu (1931) found dry, rough, pigmented skin with papuler emptions situated at the site of hair follicles on the extensor surfaces of the limbs, on the shoulders and abdomen together with xerophthalmia and keratomalacia in Chinese soldiers and they ascribed the cutaneous changes due to vitamin A deficiency.

Rapaport and his co-workers (1942) reviewed the considerations linking ichthyosis to vitamin A deficiency. They made an extensive study of several patients with ichthyosis and found frequent association in the same patient of both ichthyosis and the follicular keratotic lesions of avitaminosis A; a seasonal fluctuation of the condition with great amerlioration or complete return to normalcy during the summer in both ichthyosis and a frequent delay in the first appearance of ichthyosis until after weaning; a marked dryness of the skin in both conditions, with deficiency or absence of sweat-gland and sebaceous-gland secretions; a predilection for involvement of the same regions of the skin in both conditions; and similarity in the histological pathology of the skin.

Both xeroderma and ichthyosis are quite common in India. During the last 12 years in different teaching hospitals the author had a chance to observe quite a large number of cases/

(Lahiri, 1945) and again a large number of cases in an epidemic following refugee movement after the partition of India in 1947 (Lahiri, 1948).

(2) PHRYNODERMA: Phrynoderma or follicular keratosis was usually discovered on routine examination for some other dermatosis in apparently well-nourished people in the prisoner-of-war camp in Singapore (Sefton, 1947). Phrynoderma are papules and are conical in shape of about 4 to 6 millimetres in size and occur symmetrically on the antero-lateral aspect of limbs. Frazier and Hu (1936) pointed out that the condition first develops in a localized area and then follows rapid symmetrical involvement of the antero-lateral aspects of the thighs or posterolateral areas of the upper parts of the forearms. Other parts of the body are next implicated but hands, feet and scalp are spared.

It is again one of the very common deficiency skin conditions in the East. Although the lesion is significantly higher in poorer classes but the middle classes are by no means exempt. In India Krishma Rao (1948) surveyed amongst the university students who come from middle class and despite a moderately good diet the incidence of vitamin A defieiency among the students was found quite high. One of the responsible factors for this deficiency in the university students was the ignorance about

value of food stuffs and of what contributes a balanced or an adequate diet and also the lack of interest in his own health problems. Rao (1938) observed that malnutrition exists in the population in India chiefly because of inadequate income, poor and bad food habits, unavailability of proper foods, physiological stress without adequate increase in food and metabolic disorders and diseases which interfere with the digestion and absorption of foods.

The author had the opportunity to observe a large number of cases of phrynoderma in India after Bengal famine in 1943. A total of 422 cases were observed by the author during the period between 1944 to 1948 and these cases also showed dryness of the skin, diffused alopecia, brittleness of the nails besides phrynoderma around the elbows and above and below the knees (Lahiri, 1948). The author has seen some typical cases of phrynoderma at Glasgow in 1949 and in the same year in Eire and in Northern Ireland and also in Wales in 1950 but has not seen any cases yet in England and at Edinburgh.

(3) PITYRIASIS RUBRA PILARIS: Cases of pityriasis rubra pilaris has relationship with vitamin A has been reported by quite a large number of dermatologists like Brunsting and Shaard (1941), Peck and Chargin (1941), Leitner (1946)/

and others. Cornblect and his associates (1947) have also reported such experience. The author for the first time was convinced about the relationship in this skin condition with avitaminosis A by observing the improvement of his only case in India with a long-continued vitamin A therapy (Lahiri, 1949).

(4) DARIER'S DISEASE: A new phase in the relationship of vitamin A to cutaneous changes was inaugurated by Peck and his associates (1941) who claimed that Darier's disease is due to vitamin A deficiency.

Later on other workers have also found associations of vitamin A deficiency with Darier's disease like Leitner and Moore (1946), Leitner (1946), Moore (1946), Thomson (1946), Simpson (1947) and many others.

The author has not seen any case of Darier's disease in India and the first case he has seen being demonstrated in the Edinburgh session of the British Association of Dermatology on the 15th July 1950.

(5) PIGMENTATION OF SKIN: Tolmach and Graham (1940) have observed pigmentation of skin in avitaminosis A. Stryker and his associates (1945) reported a case where bluish pigmented patches with pruritus and eosinophilia was due/

to vitamin A deficiency. Benedek (1947) reported a large number of cases of pigmentation, amongst American soldiers returning home from the East, as due to vitamin A deficiency.

The author observed in India in 1943 after the Bengal famine and again in 1948 after the partition of Bengal resulting in mass movement of refugees, bluish pigmented macular patches with pruritus and eosinophilia associated with avitaminosis A (Lahiri, 1948 and Lahiri, 1949).

The other type of pigmentation of the skin associated with avitaminosis A is carotenemia which is yellow colouration of the skin in persons consuming excess amounts of carrots and vegetables. This condition also has been rep rted by various workers (Palmir, 1938).

(6) NUMMULAR ECZEMA: Nummular eczema is a definite entity and was first described by Devergie in 1857. Later on quite a number of workers described in different countries. But Becker and Obermayer (1940) described it and called it nummular eczema. In the latest most convincing classification of eczema it has been placed in post-traumatic infective eczema group (Percival, 1947). Gross (1941) established the relationship of nummular eczema with vitamin A deficiency.

The author had also been treating for the last several years in India nummular eczema cases with vitamin A therapy internally together with or without local treatment (Lahiri, 1949). Peterkin /

(1950) has also treated nummular eczema by vitamin A with a fairly good result.

(7) ACNE VULGARIS: Saunders (1944) who in an attempt to alleviate a mild chronic sinusitis began to take vitamin A in dose of 100,000 units daily in 1943. Vitamin A had no appreciable effect on the sinusitis. After he had taken it for 6 months he was surprised to find that on his back pustules of acne vulgaris for the first time in 21 years cured. After discontinuing acne appeared on back and disappeated after 3 months treatment and remained clear with 50,000 units daily but seborrhoic dermatitis remained unaffected by vitamin A. He also had large calluses on his sole which improved also ith vitamin A.

Improvement in acne has been observed with vitamin A therapy by Maynard (1940). Lynch and Cook (1947) studied the relationship of acne vulgaris with vitamin A and they did not observe remarkable improvement in acne with vitamin A therapy. Obermayer and Foost (1945) believe that as yet they are prepared only to state that vitamin A therapy is undoubtedly of benefit of some forms of acne vulgaris while others do not seem influenced by it.

Straumfjord (1943) treated one hundred cases of acne with high vitamin A daily for 6 months and claims that the lesions disappeared in 79 per cent of his patients.

Davidson and Sobel (1949) treated cases of acne vulgaris with good results with vitamin A therapy for 3 to 6 months. Downing (1948) has observed very/

good results with vitamin A therapy in acne with numerous comedones.

An experimental study in only 35 cases of acne vulgaris treated with vitamin A therapy has been carried out by Sovitt and Obermayer (1950). They have found that only 20 cases showed improvement out of 35 cases, 12 showed no change and 3 exhibited an increase in the severity of the lesions. The investigators concluded that the response to investigation of the vitamin A bore no consistent relation to the severity of the eruption. Improvement specially found in those who did not have comedo.

Vitamin A is another agent which appears to play an important role in the process of keratinization and Sulzberger and Baer (1949) believe that this holds true also for some cases of acne vulgaris.

It is generally accepted that acne is associated with high levels of skin lipids (Kile et al, 1950). Rosenfeld (1906) reported that the production of skin lipids is greatly increased by a diet high in carbohydrates. But Kagan and his co-workers (1950) experimentally found that higher the vitamin A concentration, the higher the lipid level.

The interesting observation made by the author during the world war II on acne vulgaris is as follows. In a group of 35 university training corps men who intended to join the Indian Royal Air Force were prescribed vitamin A to improve their vision at night. The vitamin A was given in Adexolin (Glaxo Laboratories, England) in doses of 150,000 int.unit, together with vitamin D for period of 4/

to 6 weeks. When at the end of this period the men reported they were found to have clear skin and free from acne vulgaris for which 30 were getting local treatment before vitamin A and D therapy. This gave the author a pointer in 1940 when he used cod liver oil that is vitamin A and D as a routine in acne vulgaris cases with favourable results.

It was only in 1947 that a group of patients of acne vulgaris could be treated by the author with different doses of only vitamin A - 18,000 I.U., 36,000 I.U., 72,000 I.U. daily and earlier and better results could be obtained.

Vitamin A treatment was being carried on by the author as a routine treatment in one of the teaching hospitals at Calcutta (India). Results were very encouraging in every case of acne vulgaris treated by the author in India (Lahiri, 1949).

The author has also observed good results with vitamin A in acne vulgaris in the Southern General Hospital in 1949 at Glasgow under Dr. James Sommerville of the University of Glasgow.

MISCELLANEOUS SKIN CONDITIONS POSSIBLY RELATED TO DEFECTIVE VITAMIN-A METABOLISM.

(A) DUE TO HYPO VITAMINOSIS-A: There are quite a large number of skin diseases which have been successfully treated by various workers with vitamin A therapy.

Broadly speaking this category comprises the gratifying results obtained in leukoplakia (Swift, 1936) with vitamin A therapy and also in Kraurosis/

vulvae (Swift, 1936). Peterkin (1950) observed vitamin A therapy beneficial in cases of pruritus vulvae.

Sulzberger (1942) and Urbach (1946) found vitamin A therapy beneficial in certain forms of brittleness of the nails. Favourable response with vitamin A therapy has also been observed in dermatitis papillaris capillitii (Urbach and Le Winn, 1946).

Obermayer and Foost (1945) observed, in two cases of unusually hyperkeratotic lichen simplex chronicus which had proved refractory to all forms of treatment, striking improvement to follow vitamin A therapy.

Kuipers (1931) found a definite connection between the course of seborrhoic infantile dermatitis and the vitamin A content of the blood. When vitamin A was given in doses sufficient to increase the level in the blood the cutaneous lesions promptly cleared but on the other hand, when the concentration of the vitamin A in the blood fell, the clinical picture worsened.

Straumfjord (1940) regards vernix caseosa as a manifestation of vitamin A deficiency in the newborn. He reported a number of cases in which large doses of vitamin A given to the mother during the last six months of pregnancy served to decrease the amount of vernix. Napkin rash, septic spots and external ear infections in infants are found to be due to subnutrition in vitamin A (Wright, 1947).

Senile Keratosis has also been treated with high vitamin A therapy (Sovitt and Obermayer, 1950). /

Aerodermatitis verruciformis have been treated with high vitamin A by Niedelman (1947). Siskind (1947) treated pili torti with high vitamin A and Simpson (1947) found good results with vitamin A in the treatment of hyperkeratosis follicularis et para follicularis in cutem penetrans.

Sovitt and Obermayer (1950) treated porokeratosis milbelli with vitamin A therapy and Whittle (1950) treated coilloid milium.

Familial benign chronic pemphigus of the Hailey and Hailey type has been treated with success by high vitamin A therapy (Becker, 1945; Gold. 1950).

Vitamin A therapy has been found successful in cases of nummular eczema (Groes, 1941), corns and calluses (Obermayer and Foost, 1945, Urbach, 1946), alopecia (Gill, 1946), canitis and alopecia in children (Chavarria et al, 1946), arsenical keratosis (Hall, 1946), Mal De Meleda (Brunner and Tuhrman, 1950), lichen chronicus hypertrophicus (Benedek, 1947, pigmentation (Goldsmith, 1936; Mu et al, 1937, Benedek, 1946).

Author has also reported from India satisfactory results with vitamin A therapy in brittleness of nails, alopecia, canitis, nummular eczema and in a large number of chronic macular pigmented lesions in patients living on a diet practically without any animal protein and on vitamin A deficient food (Lahiri, 1948; Lahiri, 1949). /

(B) DUE TO HYPERVITAMINOSIS-A: Low protein diet has been found valuable in removing the lesions of psoriasis and rendering them more susceptible to be removed by local application (Schamberg, 1932). Hoffmann and his associates (1947) have found psoriasis lesions markedly improved or completely cleared within a certain period of time after a diet restricted in both carotene and vitamin A. During the Bengal famine in 1943 the author has not seen a single case of psoriasis or lichen planus in one of the largest skin clinics in India and has always prescribed low vitamin A diet to psoriatics as a routine (Lahiri, 1945).

E X P E R I M E N T A L

The experimental part of the present investigation on the "Role of Vitamin A in Certain Skin Diseases" has been considered under the following headings:-

A. Laboratory estimation of carotene and Vitamin A
   (1) In normal human subjects - 114 persons.
   (2) In patients with skin diseases supposed to be related to vitamin A nutrition - 170 patients.
   (3) In patients during follow-up.

B. Vitamin A clearance test in normal subjects to determine the maximum absorption time with adminstration of vitamin A orally and again parenterally to ascertain the vitamin A utilisation.

C. Vitamin A clearance test in patients of skin diseases due to avitaminosis A to find out any descripency in vitamin A utilisation.

D. Laboratory estimation of 24 hours urine to estimate the excreted androgens.

E. Experiments with vitamin A therapy in cases of skin diseases supposed to be due to avitaminosis A.

ASSAY OF VITAMIN-A NUTRITION

Laboratory methods for assessment of vitamin A states of the body are numerous. Among these the determination of the concentration of the blood is the most valuable.

METHODS ADOPTED IN THE PRESENT INVESTIGATION

Laboratory method supported by clinical improvement in the follow-up cases of skin diseases with vitamin A Therapy, in most of the cases, have been followed.

This method has been supported by other workers. Marrack (1948) believes that investigation of vitamin A is an indicator of the state of vitamin A nutrition. He also believes that laboratory methods as contrasted with clinical appraisal, supply impersonal data, free of temperamental bias and their meaning have same world over.

BLOOD VITAMIN-A ESTIMATION

There are several methods for the estimation of vitamin A in the blood. The most usual method is that of Carr-Price (1939). This method has further been modified by various workers such as Bessey et al (1946) and Kramer et al (1947).

The method used in the present investigation is that of Kramer and his associates (1947) with further modification as regards quantity of blood and the type of instrument. In the present/

present work 2 c.c. of serum being used and arrangements have been made to estimate eight different samples of blood together by special fitting of an apparatus (Fig. No. 1 - Page 51). A very sensitive instrument has been used as advised by Dr. C.P. Stewart (1949). The instrument is a Diffraction Grating Spectrophotometer made by Unicam Instrument (Cambridge) Ltd., Cambridge, England (Fig. No. 2 - Page 51).

Recently a new colorimetric method has been devised by Sobel and Snow (1947) for the estimation of vitamin A with activated glycerol dichlorhydrin. This method is called the GDH method. This method has further been modified in the present work by taking 2 c.c. of serum and using the Diffraction Grating Spectrophotometer (Unicam) as advised by Stewart (1949).

The Carr-Price method has been compared with GDH method. Both these methods are almost the same in principle except that different reagents in different quantities have been used at different wave lengths of the Unicam.

In the same sample of blood both carotene and vitamin A are estimated. The method of estimation of carotene is the same by both the methods. For the interference of carotene by the Carr-Price method Antimony trichloride is added and readings taken on the Unicam at 615 mu wave length while in case of the GDH method activated glycerol dichlorhydrin is added and readings taken on the Unicam at 440 mu wave length.

Before/

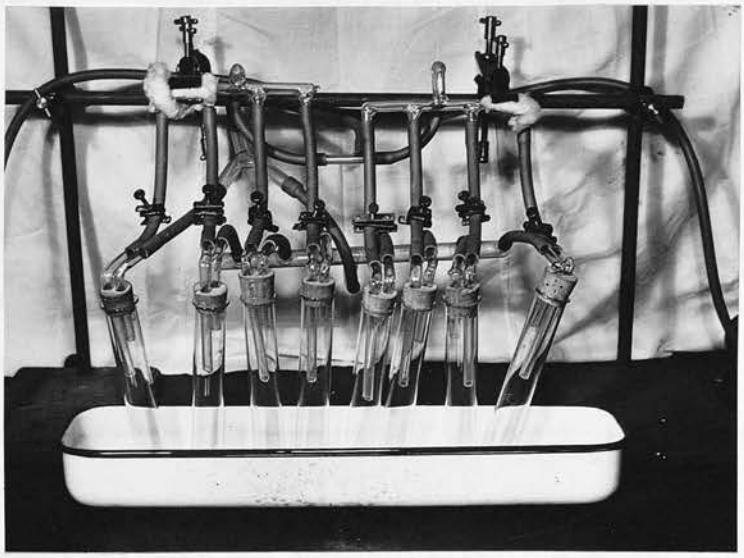


Fig. No. 1. Arrangement of apparatus to pass nitrogen gas through 8 samples.

Fig. No. 2. Special Diffraction Grating Spectrophotometer (Unicam).

Before commencing the experiments with blood standard curves were prepared with standard carotene and standard vitamin A (Standard carotene and vitamin A were supplied by the Medical Research Council, London).

STANDARD CAROTENE AND VITAMIN-A CURVES

Standard carotene and standard vitamin A curves are necessary to determine the amount of carotene and vitamin A in international units from the optical density of the sample of blood to be investigated.

Two different vitamin A curves namely one for the Carr-Price method and the other for the GDH method are necessary.

Two different interference curves for carotene for different methods are also necessary.

METHOD OF PREPARATION OF CURVES WITH STANDARDS

The different curves prepared with standard substances supplied by the Medical Research Council, London are:-

(1) Standard vitamin A curve by using antimony trichloride.

(2) Standard vitamin A curve by using activated glycerol dichlorhydrin.

(3) Carotene curve.

(4) Carotene Interference curve using antimony trichloride.

(5) Carotene Interference curve using activated glycerol dichlorhydrin.

STANDARD/

STANDARD VITAMIN-A CURVES

Known solutions of standard vitamin A of different dilutions have been prepared in the following way:-

Standard vitamin A capsule containing 2,500 international units of vitamin A is opened in chloroform and is made up to 10 c.c. with chloroform.

10 c.c. of the vitamin A in chloroform solution contains 2,500 I.U. vit. A.

1 c.c. " " " " " " " " 250 " " "

This solution is further diluted to 10 c.c. by adding chloroform. Therefore 1 c.c. of this rediluted solution contains 25 I.U. of vitamin A. Taking different quantities of this solution in different test tubes and mixing with chloroform various dilutions made (Table No. 1 - page 53).

Table No. 1

Preparation of different known dilutions of standard vitamin A

International units of vit. A	1·25	2·5	5·0	7·5	10·0
Quantity in c.c. of vit. A solution taken	0·05	0·1	0·2	0·3	0·4
Quantity in c.c. of chloroform added to make 1 c.c.	0·95	0·9	0·8	0·7	0·6

Two sets of each of the above solution are prepared in standard test tubes supplied with Unicam for finding out the optical density by the instrument using 615 mu wave length and adding to

each/

each of the solutions 3 c.c. of antimony trichloride from a dropping pippet and also to find out the optical density by using 550 mu wave length and adding 4 c.c. activated glycerol dichlorhydrin.

ANTIMONY TRICHLORIDE: Unicam is switched on half an hour before taking readings to warm up the instrument. In a standard tube (supplied with Unicam) is poured 1 c.c. of chloroform and 3 c.c. of antimony trichloride and is placed in the "well" of the instrument and the spot of light on the scale is adjusted at "0". This standard tube is removed from the well and standard tubes containing known strength of vitamin A in solution is placed in the well and 3 c.c. of antimony trichloride is added when immediately blue colour develops. After about two seconds the spot of light will be shady on the scale for a couple of seconds when reading is taken and gradually colour fades and the spot of light moves towards zero on the scale. Optical density using different strengths of vitamin A solution (Table No. II - page 54).

Table No. II.

Optical density measured by Unicam of solutions of known strengths after addition of antimony trichloride.

Standard solution containing vit. A in I.U.	- 1·25	- 2·50	- 5·0	- 7·5	- 10·0
Instrumental Reading showing optical density	- 0·020	- 0·045	- 0·090	- 0·135	- 0·18

STANDARD/

STANDARD VITAMIN-A CURVE: With the optical density as the abscissa and the known strength in international units of vitamin A as the co-ordinate a curve is drawn on a graph paper. The vitamin A curve is a straight line (Fig. No. 3 - page 57).

ACTIVATED GLYCEROL DICHLORHYDRIN: The wave length of the Unicam is changed to 550 mu. In a standard test tube (supplied with Unicam) is poured 1 c.c. of chloroform and 4 c.c. of activated glycerol dichlorhydrin and having placed in the well of the instrument the spot of light on the scale is adjusted at "0". Then the standard tubes containing known strengths of vitamin A in solution are placed in the well and 4 c.c. of activated glycerol dichlorhydrin is added when pink colour develops immediately which maintains its intensity for half an hour as found out by taking readings every 5 minutes for 12 times. But for experimental purpose the readings are taken within 5 minutes. Optical density using different strength of vitamin A solution is shown in the Table No. LLI.

Table No. III.

Optical density measured by Unicam of solutions of known strengths after addition of activated glycerol dichlorhydrin.

Standard solution
containing vit. A - 1·25 - 2·50 - 3·125 - 5·0 - 6·25 - 7·5 - 9·375 - 12·50

Instrument Reading
showing optical density - 0 - 0.006 - 0.009 - 0.018 - 0.025 - 0.025 - 0.028 - 0.038 - 0.052

STANDARD

STANDARD VITAMIN-A CURVE: With optical density as the abscisa and the known strength in international unit of vitamin A as the co-ordinate a curve on a graph paper is drawn. The vitamin A curve is a straight line (Fig. No. 4 - page 58).

STANDARD CAROTENE CURVE

Standard carotene is dissolved in chloroform and solutions prepared of different strengths as follows. The different solutions are poured in different standard test tubes and optical density of known solutions are found out at 440 mu wave length on Unicam.

Table IV.

Showing different dilutions of carotene in international units and the corresponding optical density

Concentration of carotene	- 0·5	- 1·0	- 1·5	- 2·0	- 2·5	- 3·0	- 3·5	- 4·0	- 4·5	- 5·0
optical density	- 0·25	- 0·047	- 0·07	- 0·095	- 0·118	- 0·14	- 0·16	- 0·185	- 0·207	- 0·230

STANDARD CAROTENE CURVE: With optical density as the abscisa and the known strength of carotene in international unit as the co-ordinate a curve on a graph paper is drawn. The carotene curve is a straight (Fig. No. 5 - page 60).

CAROTENE INTERFERENCE CURVES.

Two separate carotene interference curves are drawn - one for the GDH method and the other for the Carr-Price method.

The/

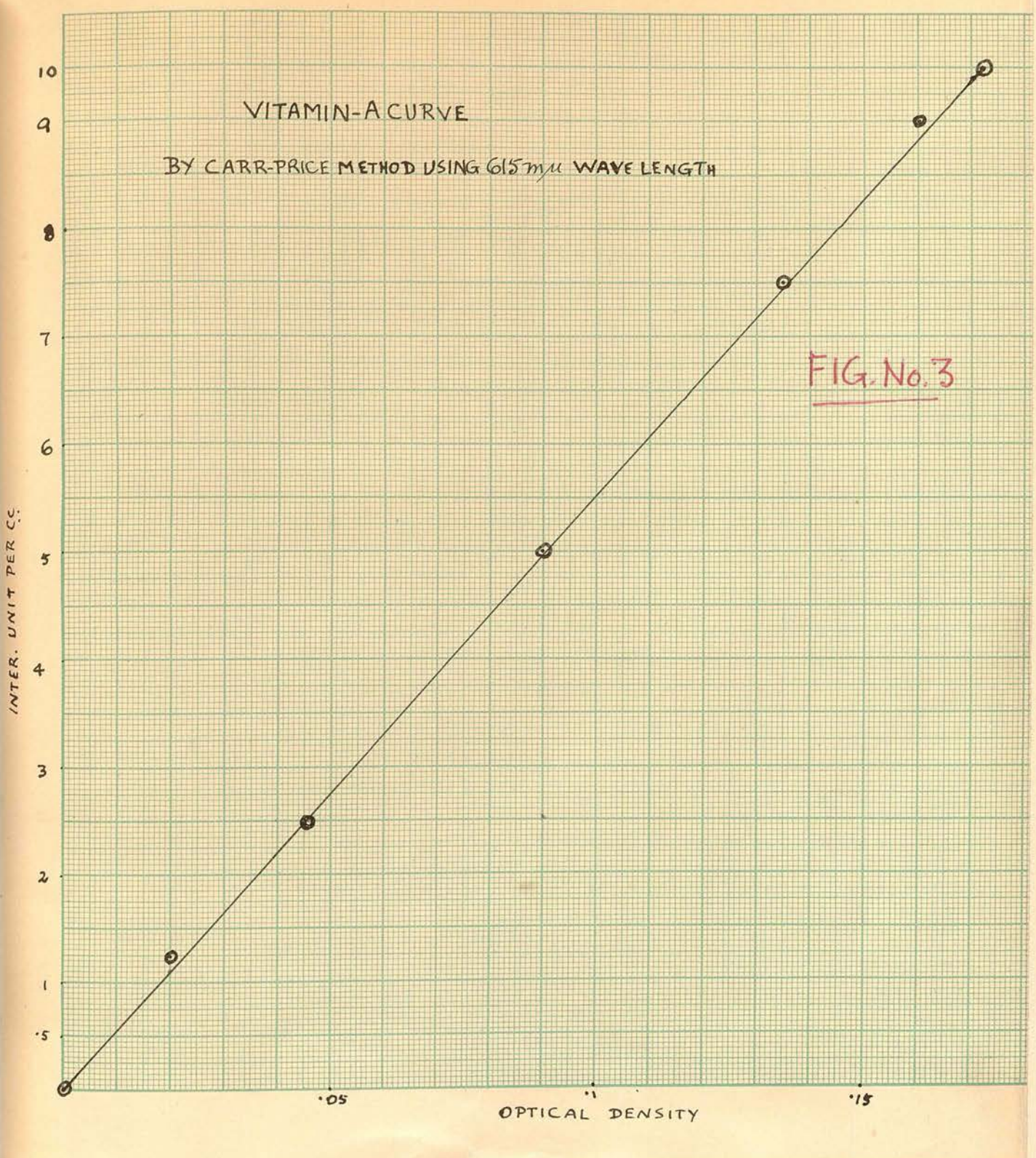


Fig. No. 3 Standard vitamin A curve by Carr-Price method.

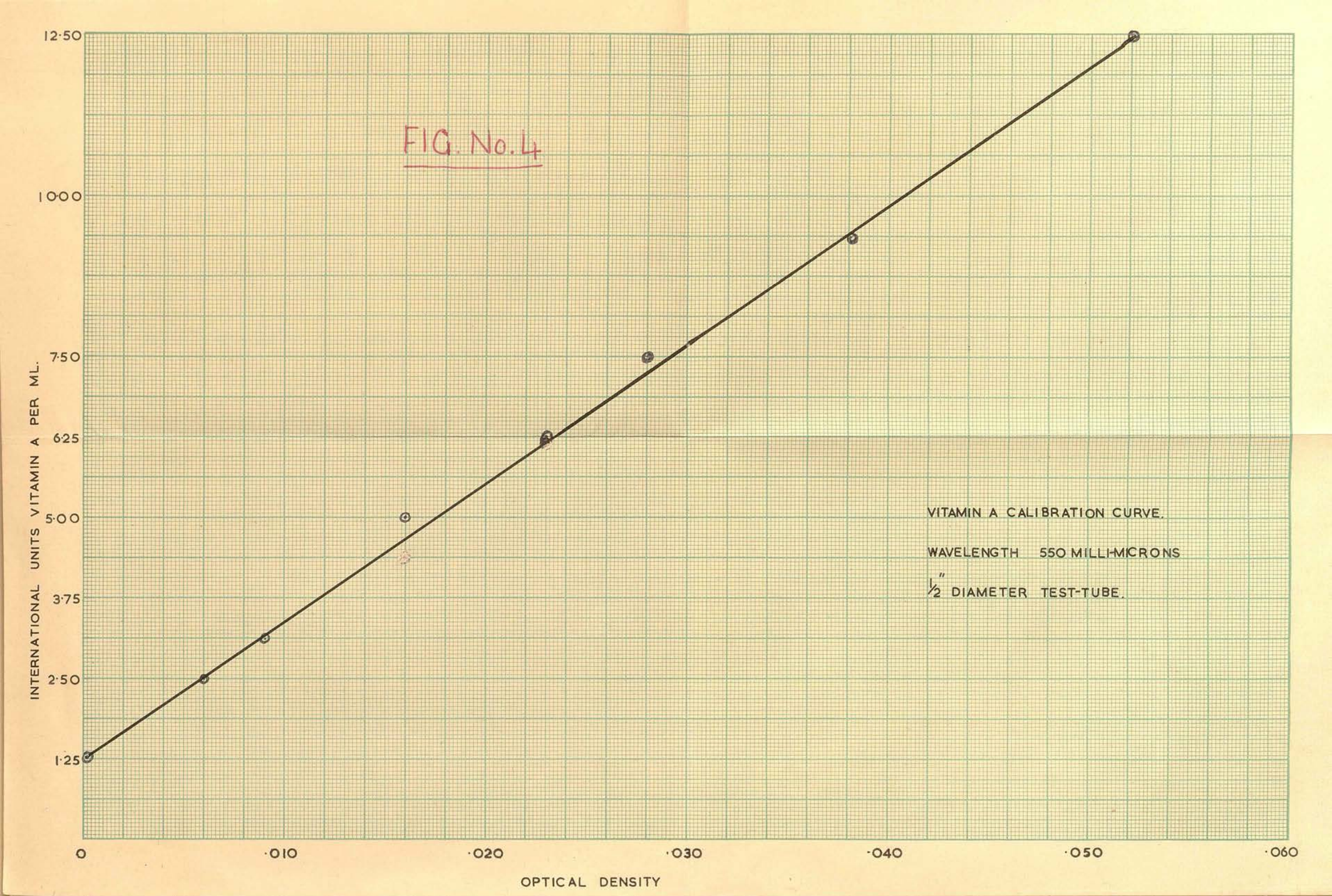


Fig. No. 4 Standard vitamin A curve by GDH method.

The graphs are drawn in the same manner as that of vitamin A, carotene being substituted for vitamin A in concentration of from 1 to 10 I.U. per c.c. of solution. These graphs are used to correct the vitamin A reacting at 550 mu when activated glycerol dichlorhydrin is used and at 615 mu when antimony trichloride is used

From the optical density at 440 mu the carotene is found (with the carotene graph as in(Fig. No. 5 - page 60). The optical density which this amount of carotene will produce at 550 mu and at 615 mu respectively are found from the carotene interference graph. The optical density is subtracted from the Total optical density. From the corrected 550 mu and 615 mu respectively, the vitamin A concentration is found on the vitamin A graph.

METHOD: For the GDH method solution of carotene prepared of following strengths and adding 4 c.c. of activated glycerol dichlorohydrin the readings are taken on the Unicam at 550 mu wave length (Table No. V - page 59).

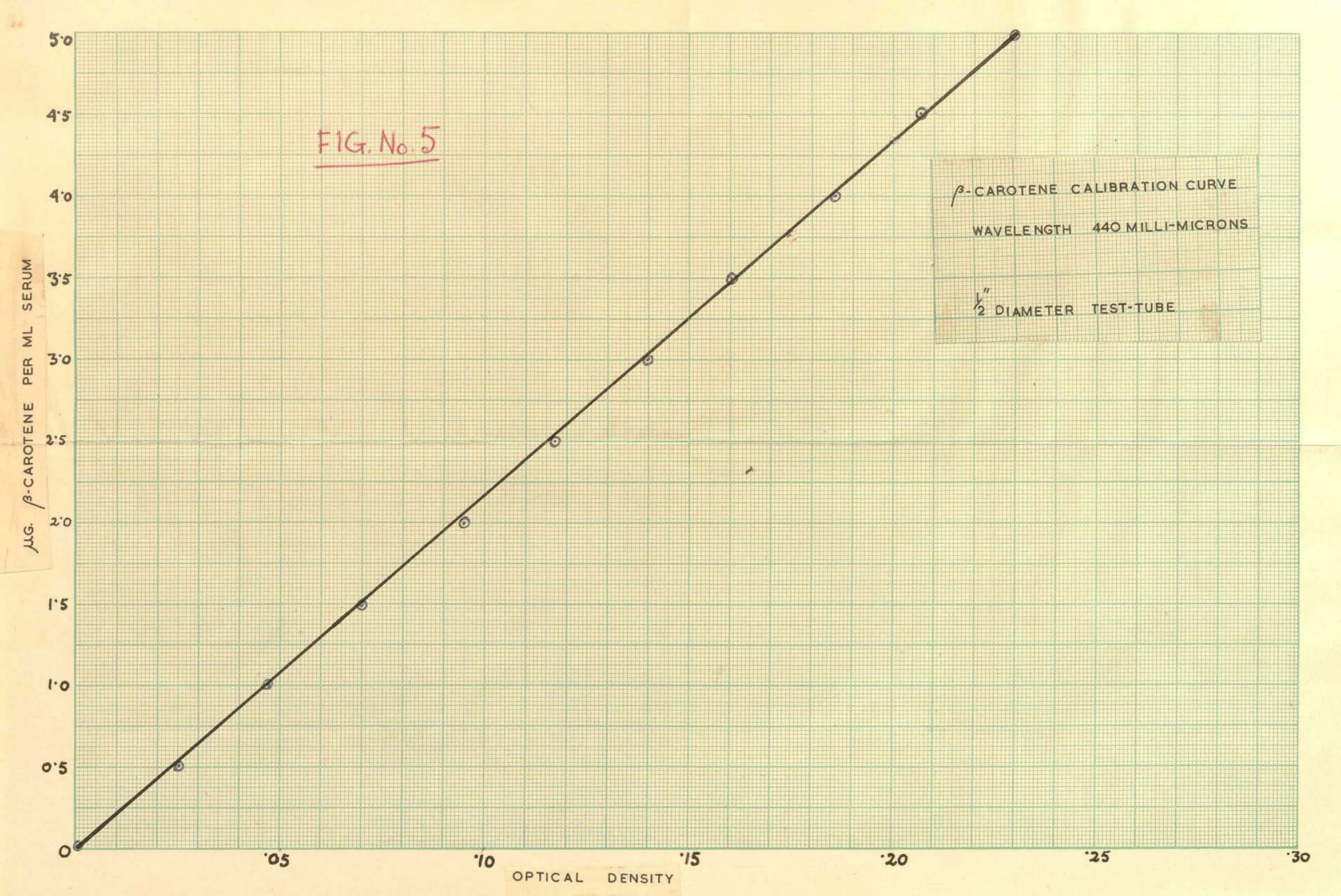
Table No. V.

Carotene solution	- 100 I.U.	- 200 I.U.	- 300 I.U.	- 400 I.U.
Instrumental Redding	- 0.001	- 0.0052	- 0.009	- 0.017

CAROTENE INTERFERENCE CURVE FOR GDH METHOD.

With/

FIG. No. 5


β-CAROTENE CALIBRATION CURVE
WAVELENGTH 440 MILLI-MICRONS
½" DIAMETER TEST-TUBE
μG. β-CAROTENE PER ML SERUM
5·0
4·5
4·0
3·5
3·0
2·5
2·0
1·5
1·0
0·5
0
·05
·10
·15
·20
·25
·30
OPTICAL DENSITY

The carotene interference curve is a curved line as shown in Fig. No. 6 by GDH method using 550 mu wave length.

CAROTENE INTERFERENCE CURVE FOR CARR-PRICE METHOD.

With the carotene solution in the standard tubes interference is found out with a changed wave length of 615 mu and by mixing 3 c.c. of antimony trichloride with each known dilution of carotene solution and readings taken (Table No. VI page 61).

Table No. VI.

Carotene concentration and optical density at 615 mu.

Carotene solution	- 100 I.U.	- 200 I.U.	- 400 I.U.
Instrumental Reading	- 0•008	- 0•018	- 0•036

The curve is drawn as before which is a straight curve as shown in Fig. No. 7.

CAROTENE AND VITAMIN-A ESTIMATION IN BLOOD OF NORMAL HUMAN SUBJECTS.

In the present investigation carotene and vitamin A have been estimated by GDH and also by Carr-Price methods. For experiments about 5 c.c. venous blood is drawn and when clot forms 2 c.c. of serum is drawn off.

Estimation have been carried on unsaponified and also on saponified serum using both the methods. Procedure being the same for both the methods.

REAGENTS REQUIRED: (1) Absolute alcohol (2) Petroleum ether, (3) Nitrogen gas (4) chloroform (5) Activated glycerol dichlorhydrin/

and away from any vibration and brilliant light.

USE OF THE INSTRUMENT: Inserted in the "well" the O•N 12 Didymium filter holder with the locating pin at 90° to its Keyway as this prevents the light beam from falling on the switch. Switch knob is rotated to "ON" position and the spot of light is watched on the galvanometer scale and is adjusted to "0" by adjusting another knob. on the top of the galovanometer which is marked "ZERO ADJUST".

ESTIMATION BY GDH METHOD

2 c.c. serum is taken in a graduated centrifuge glass tube and 2 c.c. of absolute alcohol is added and mixed by tilting the tube several times. To the mixture of solution is added 4 c.c. of petrol ether (40 to 60° c) slowly and the tube containing the serum is shaken at the same time. The tube is corked and placed in the electric shaker for 15 minutes and then the tube is centrifuged for 30 seconds. The layer of petroleum ether is transferred to a calibrated test tube and petroleum ether is added to bring the volume to 4 c.c.

CAROTENE: The wave length of Unicam is adjusted to 440 mu for carotene measurement. Another standard tube (supplied with Unicam) is filled with 4 c.c of petrol ether and is placed in the well of the instrument and the knob marked "INCREASED LIGHT"/

LIGHT" is adjusted until galvanometer index reads "0" on the density scale. The tube is removed and the carotene solution is poured in another dry standard test tube and placed in the well of Unicam. The instrument reading is taken. With this optical density the amount of carotene is found out from the graph (Fig. No. 5 - page 60) in 2 c.c. of serum and thus carotene in 100 c.c. of blood is found out.

VITAMIN-A: The solution in which carotene has been determined is poured in a hard glass test tube and is placed in a water bath containing warm water at 40 to 50° c. Through the solution in the hard glass test tube nitrogen gas is passed until the tube is dry. By special arrangement as shown (Fig. No. 1 - page 51) nitrogen gas can be passed through eight samples. 1 c.c. of chloroform is now poured into the dry hard glass test tube and shaken. A blank is prepared by pouring in one of the standard test tubes 1 c.c. of chloroform and 4 c.c. of activated glycerol dichlorhydrin and is placed in the well of the Unicam and the instrument is adjusted by bringing the spot of light on "0" of the scale. This test tube is removed and in another standard test tube is poured the solution from the hard glass test tube and reading is taken on the scale. This gives the total optical density both due to vitamin A and carotene. Reading for carotene interference is/

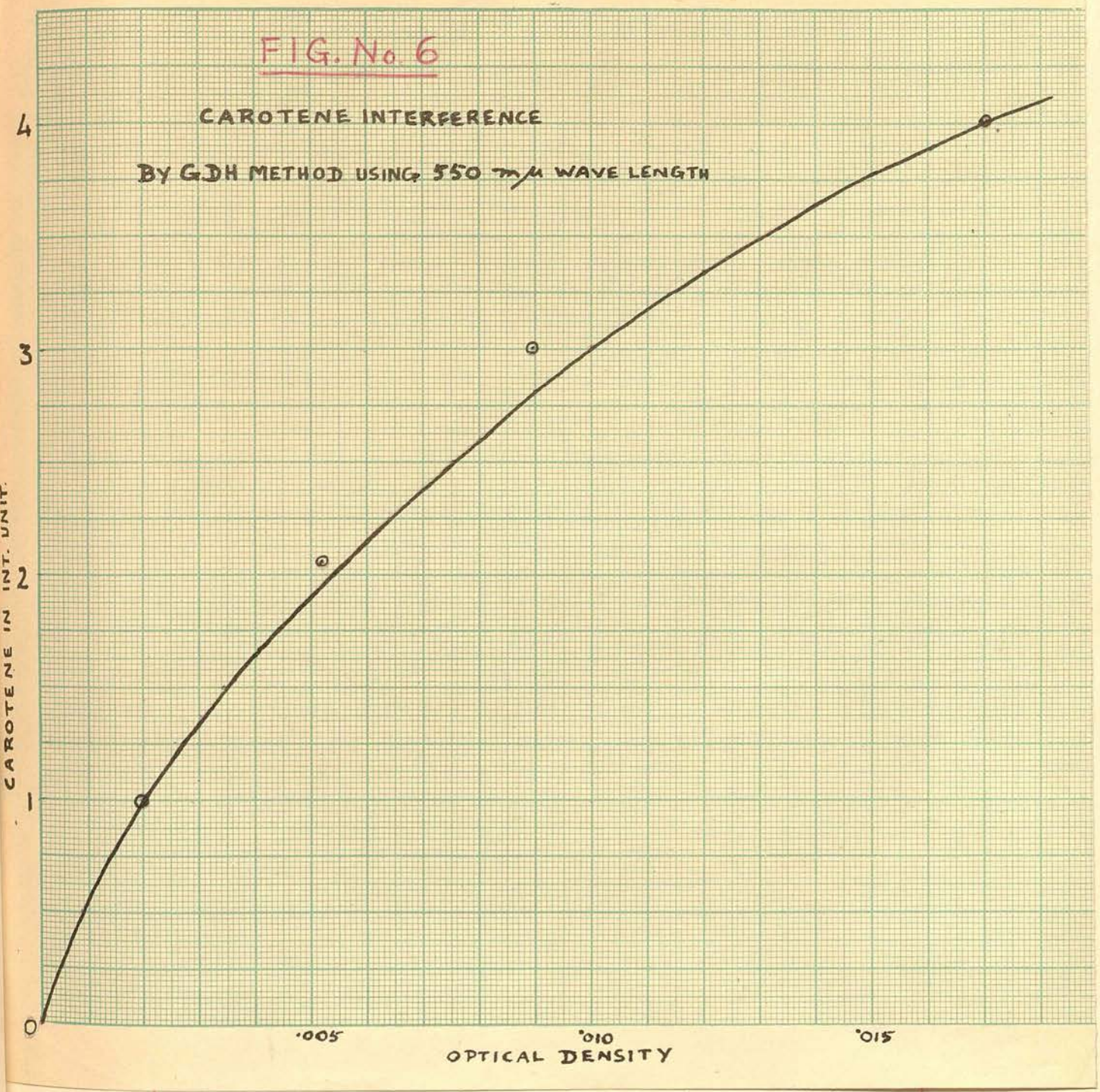


Fig. No. 6 Carotene Interference Curve by GDH method.

is obtained from the carotene interference curve (Fig. No. 6 page 65) and this is subtracted from the total optical density when true reading for vitamin A is obtained. From the standard vitamin A curve (Fig. No. 4 - page 58). Vitamin A in 2 c.c. of serum is thus found out which is converted into vitamin A in international unit per 100 c.c. of blood.

ESTIMATION BY CARR-PRICE METHOD.

Is done exactly in the same manner. When dry 1 c.c. of chloroform is poured in the hard glass test tube and shaken. Then a blank is prepared in a standard test tube by pouring 1 c.c. chloroform and 3 c.c. antimony trichloride and placing in the well of the Unicam. The spot of light is adjusted at "0" of the scale and the blank is removed. The solution in the hard glass tube is poured into a standard test tube and placed in the well of Unicam. From a burette 3 c.c. antimony trichloride is poured in when blue colour develops and the spot of light moves and after a couple of seconds becomes steady for about another couple of seconds when reading is taken quickly as by the fifth second the blue colour starts fading and the spot of light moves towards "0" of the scale.

This reading gives the total optical density for vitamin A and carotene in serum. Interference for carotene is obtained from the carotene interference curve (Fig. No. 7 - page 68) and is subtracted from the total optical density which gives the true reading for vitamin A by Carr-Price method. From the standard/

standard vitamin A curve (Fig. No. 3 - page 56). Vitamin A is found out which is the value in 2 c.c. of serum. This is then converted for 100 c.c. of blood.

SAPONIFICATION: Estimates of vitamin A by Carr-Price method has been done by various workers. Bessey and his co-workers (1946) for the first time saponified the serum for 20 minutes before finding out the vitamin A value. In the present work serum has been saponified for different lengths of time such as 0, 20, 30, 40, 50, 60 and 90 minutes (Scandrett, 1949) and then carotene and vitamin A values have been found out (Table No. VII page 71). A curve has been drawn with different vitamin A values of the same serum when saponified for different lengths of time (Fig. No. 8 - page 70).

Since in the present work maximum vitamin A values have been found out when serum is saponified for 60 minutes the experiment is repeated with the same serum (as used for Table No. VII).

By using the same blood (as for Table No. VII) carotene and vitamin A have been estimated by Carr-Price method (Table No. VIII - page 72).

By using the same blood (as for Table No. VII) carotene and vitamin A have been estimated after saponifying the serum for 20 minutes (Table No. IX - page 73) by Carr-Price method and also after saponifying the same serum (as for Table No. VII - page 71) for 60 minutes (Table No. X - page 74) by Carr-Price method.

By/

FIG. No. 7

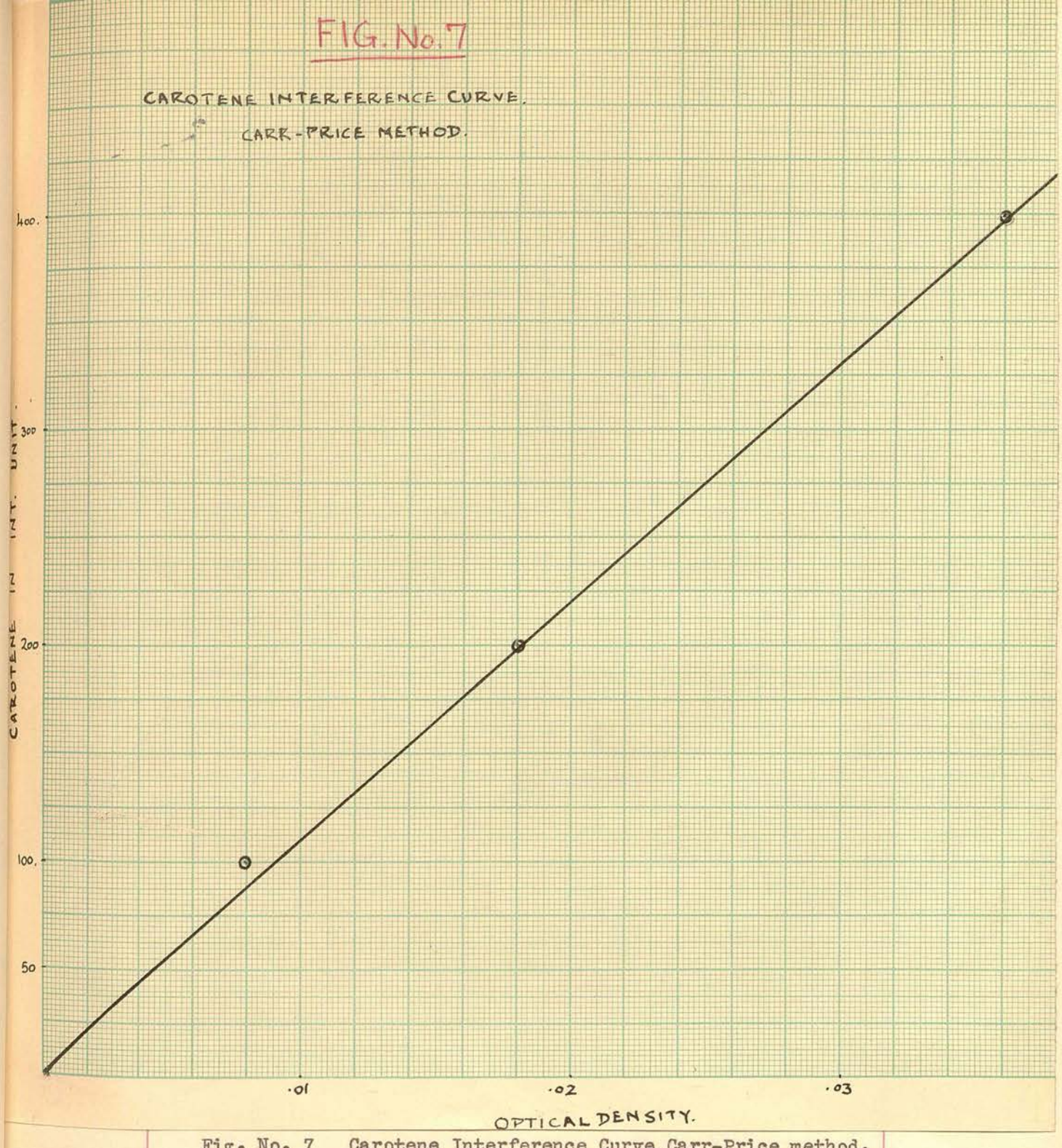


Fig. No. 7 Carotene Interference Curve Carr-Price method.

By using the same serum (as for Table No. VII on page 71) carotene and vitamin A have been estimated by GDH method before saponification (Table No. XI - page 75) and after saponifying for 60 minutes (Table No. XII - page 76).

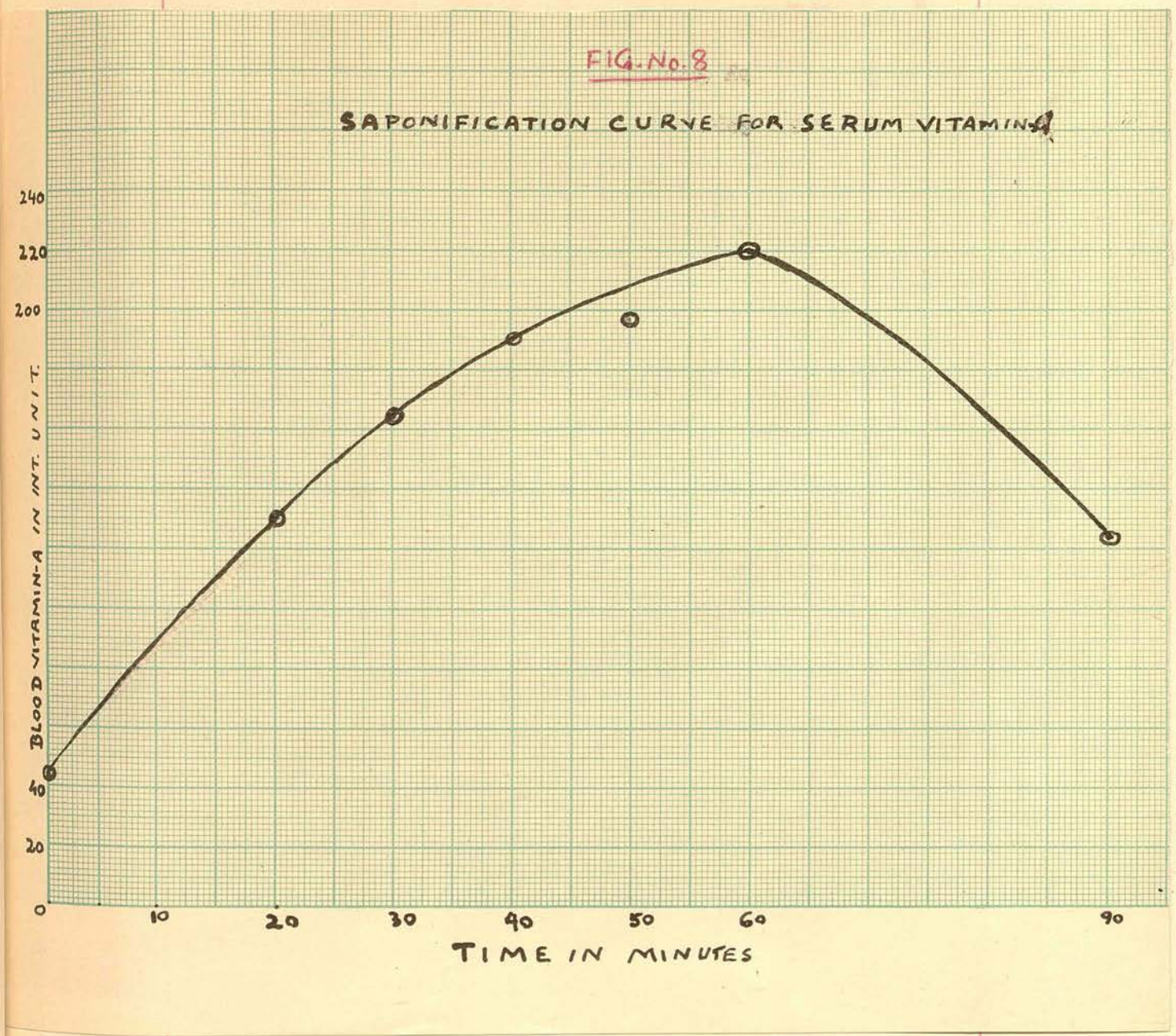


Fig. No. 8 Saponification curve for serum vitamin A by Carr-Price method.

Table No. VII.

Vitamin A and carotene estimation of the same sample of blood before and after saponifying serum for 20, 30, 40, 50, 60 and 90 minutes by Carr-Price.

Time in minute	Inst. Read-ing for carot.	Carot. in 2 cc. serum	Carot. in I.U. in 100 cc. serum	Inst. Read-ing for vit A	Interference for vit. A	True Read-ing for vit.A	Vit. A in 2 cc. serum	Vit.A in I.U. in 100 cc. serum
'0' minutes	0•019	0•43	21•5	0•020	0•004	0•160	0•90	45•0
20 "	0•026	0•59	29•5	0•055	0•00105	0•05395	2•72	13•0
30 "	0•026	0•59	29•5	0•065	0•00165	0•06395	3•28	164•0
40 "	0•026	0•59	29•5	0•074	0•00105	0•07295	3•79	189•5
50 "	0•026	0•59	29•5	0•077	0•00105	0•07595	3•95	197•5
60 "	0•026	0•59	29•5	0•085	0•00105	0•08393	4•40	220•0
90 "	0•026	0•59	29•5	0•052	0•00105	0•05195	2•57	123•5

Table No. VIII.

Blood vitamin A and carotene estimation done 4 times in the same blood (as used for Table No. VII) using Carr-Price method with unsaponified blood.

Sample No.	Inst. Read-Carot. for carot.	Carot. in I.U. 2 cc. serum	Carot. in I.U. 100 cc. serum	Inst. Read-Interference for vit.A	True Read-Vit. A in for carot.	Vit. A in I.U. for vit.A	Vit. A in I.U. 2 cc. serum	Vit. A in I.U. 100 cc. serum
1.	0.019	0.43	21.5	0.020	0.004	0.16	0.90	45.0
2.	0.019	0.43	21.5	0.026	0.004	0.22	1.20	60.0
3.	0.018	0.40	20.0	0.026	0.0037	0.0223	1.25	62.5
4.	0.019	0.43	21.5	0.024	0.004	0.020	1.10	55.0
		mean	21.12				mean	55.62

Table No. IX.

Blood vitamin A and carotene estimation done 4 times in the same serum (as used for Table No. VII & VIII) using Carr-Price method after saponifying serum for 20 minutes.

Sample No.	Inst. Read for carot.	Carot. in 2 cc. serum	Carot in 100 cc. serum	Inst. Read for vit.A	Interference for carot.	True Read for vit.A	Vit. A in 2 cc. serum	Vit. A in I.U. in 100 cc. serum
1.	0.026	0.59	29.5	0.055	0.00105	0.05395	2.72	131.0
2.	0.026	0.59	29.5	0.055	0.00105	0.05395	2.72	131.0
3.	0.026	0.59	29.5	0.055	0.00105	0.05395	2.72	131.0
4.	0.026	0.59	29.5	0.055	0.00105	0.05395	2.72	131.0
		mean -	29.5				mean -	131.0

Table No. X.

Vitamin A and carotene estimation done 4 times in the same serum (as used for Table No. VII) by Carr-Price method after saponifying for 60 minutes.

Sample No.	Inst. Read for carot.	Carot. in 2 cc. serum	Carot. in 100 cc. serum	Inst. Read for vit. A	Interference for carot.	True Read for vit. A	Vit. A in 2 cc. serum	Vit. A in I.U. in 100 cc. serum
1.	0.026	0.59	29.5	0.085	0.00105	0.08393	4.40	220.0
2.	0.026	0.59	29.5	0.085	0.00105	0.08393	4.40	220.0
3.	0.026	0.59	29.5	0.085	0.00105	0.08393	4.40	220.0
4.	0.026	0.59	629.5	0.085	0.00105	0.08393	4.40	220.0
			mean - 29.5					mean - 220.0

Table No. XI.

Vitamin A and carotene estimation done 4 times in the same sample of blood (as used for Table VII) by GDH method unsaponified serum.

1.	-	0·024	-	0·50	-	25·00	-	0·017	-	0·0009	-	0·0161	-	4·63	-	231·5
2.	-	0·024	-	0·50	-	25·00	-	0·017	-	0·0009	-	0·0161	-	4·63	-	231·5
3.	-	0·024	-	0·50	-	25·00	-	0·017	-	0·0009	-	0·0161	-	4·63	-	231·5
4.	-	0·024	-	0·50	-	25·00	-	0·017	-	0·0009	-	0·0161	-	4·63	-	231·5
					Mean	-	25·00							mean	-	231·5

Table No. XII.

Vitamin A and carotene estimation done 4 times in the sample of blood (as used for Table VII) by GDH method after saponifying serum for 60 minutes.

Sample No.	Inst. Read for carot.	Carot. in 2 cc. serum	Carot. in I.U. 100 cc. serum	Inst. Read for vit. A	Interference for carot.	True Read for vit.A	Vit. A in 2 cc. serum	Vit. A in I.U. 100 cc. serum
1.	0.030	0.52	26.00	0.018	0.0010	0.0170	4.8	240.0
2.	0.030	0.52	26.00	0.018	0.0010	0.0170	4.8	240.0
3.	0.030	0.52	26.00	0.018	0.0010	0.0170	4.8	240.0
4.	0.030	0.52	26.00	0.018	0.0010	0.0170	4.8	240.0
		mean	26.00				mean	240.0

The GDH method with unsaponified serum has been adopted in the present investigation for the estimation of vitamin A nutrition of 114 normal human subjects (Table No. XIII - page 78 and No. IV - page 82) and also in patients with various skin diseases where vitamin A is supposed to be responsible such as are:-

1. In 75 cases of Acne Vulgaris (Table No. XV - page 87)
2. " 9 " " Ichthyosis (Table No. XVI - page 92)
3. " 1 " " Pityriasis rubra pilaris (Table No. XVII - page 93)
4. " 15 " " Nummular Eczema (Table No. XVIII - page 94)
5. " 16 " " Benis's Prurigo (Table No. XIX - page 96)
6. " 7 " " Neurodermatitis (Table No. XX - page 98)
7. " 7 " " Alopecia Areata (Table No. XXI - page 99)
8. " 6 " " LUpus Erythematosis (Table No. XXII - page 100)
9. " 2 " " Keratoderma Palmaris et Plamtaris (Table No. XXIII - page 100
10. " 15 " " Lichen Planus (Table No. XXIV - page 101)
11. " 17 " " Psoriasis (Table No. XXv - page 102)

Table No. XIII

ESTIMATION OF CAROTENE AND VITAMIN-A IN BLOOD OF NORMAL ADULTS.

MALES

No.	Instrumental Reading for Carotene	Carotene in 2 cc. serum	Carotene in I.U. in 100 cc. serum	Inst. Reading for vit. A	Interference for carotene	True Reading for carotene	Vitamin A in 2 cc. serum	Vitamin A in I.U. in 100 cc. serum
1.	0•064	1•40	70•0	0•020	0•0032	0•0168	4•875	234•7
2.	0•072	1•50	75•0	0•015	0•00355	0•01145	3•750	187•5
3.	0•062	1•30	65•0	0•020	0•0029	0•0171	4•938	246•9
4.	0•076	1•65	87•5	0•019	0•004	0•015	4•500	225•0
5.	0•063	1•35	67•5	0•007	0•003	0•004	2•125	106•2
6.	0•047	1•00	50•0	0•009	0•002	0•007	2•800	140•0
7.	0•051	1•10	55•0	0•020	0•0023	0•0177	5•062	253•1
8.	0•038	0•80	40•0	0•015	0•0015	0•0135	4•188	209•4
9.	0•040	0•85	42•5	0•017	0•0016	0•0134	4•155	207•7
10.	0•066	1•45	72•5	0•020	0•0034	0•0166	4•870	243•5
11.	0•063	1•35	67•5	0•016	0•003	0•013	4•07	203•5
12.	0•050	1•10	55•0	0•018	0•0023	0•0157	4•63	231•5
13/								

13.	0•069	1•47	73•5	0•016	0•00345	0•01255	3•89	194•5
14.	0•087	1•87	93•5	0•012	0•00495	0•00705	2•812	140•6
15.	0•053	1•13	56•5	0•015	0•0024	0•0126	4•00	200•0
16.	0•050	1•10	55•0	0•016	0•0023	0•0137	4•65	232•5
17.	0•053	1•13	56•5	0•012	0•0024	0•0096	3•312	165•6
18.	0•096	2•07	103•5	0•017	0•0057	0•0113	3•812	190•6
19.	0•082	1•77	88•5	0•022	0•00455	0•01745	5•05	252•5
20.	0•053	1•13	56•5	0•012	0•0024	0•0096	3•312	165•6
21.	0•052	1•10	57•5	0•009	0•0023	0•0067	2•69	134•5
22.	0•080	1•70	85•0	0•017	0•0042	0•0128	4•03	201•5
23.	0•078	1•65	82•5	0•013	0•0040	0•0090	3•24	162•2
24.	0•044	0•94	47•0	0•006	0•0019	0•0041	2•187	109•3
25.	0•049	1•05	52•5	0•014	0•0022	0•0128	4•03	201•5
26.	0•056	1•20	60•0	0•015	0•0026	0•0124	3•93	196•5
27/								

27.	0.038	0.82	41.0	0.018	0.0015	0.0165	4.812	240.6
28.	0.042	0.92	45.0	0.019	0.0018	0.0172	5.00	250.0
29.	0.056	1.20	60.0	0.017	0.0026	0.0144 4 375	4.375	218.7
30.	0.038	0.82	41.0	0.021	0.0015	0.0195	5.4	270.0
31.	0.061	1.32	66.0	0.016	0.0030	0.0130	4.125	206.2
32.	0.077	1.65	82.5	0.018	0.0041	0.0139	4.25	212.5
33.	0.091	1.96	98.0	0.019	0.0053	0.0137	4.06	203.0
34.	0.075	1.62	81.0	0.008	0.0040	0.0040	2.125	106.2
35.	0.083	1.80	90.0	0.019	0.0047	0.0047	0.0143	216.5
36.	0.056	1.20	60.0	0.014	0.0026	0.0114	3.72	186.0
37.	0.070	1.50	75.0	0.015	0.0035	0.0115	3.75	187.5
38.	0.085	1.82	91.0	0.009	0.0048	0.0042	2.187	109.3
39.	0.077	1.65	92.5	0.016	0.0041	0.0119	3.875	193.7
40.	0.091	1.96	98.0	0.026	0.0052	0.0208	5.75	287.5
41.	0.040	0.85	42.5	0.016	0.0016	0.0044	2.25	112.5

42/

42.	0•062	1•32	66•0	0•016	0•003	0•013	4•025	201•2
43.	0•060	1•30	65•0	0•007	0•0029	0•0041	2•126	106•3
44.	0•070	1•50	75•0	0•016	0•0035	0•0125	4•00	200•0
45.	0•054	1•15	57•0	0•018	0•00245	0•00555	2•44	122•0
46.	0•040	0•85	42•5	0•017	0•0016	0•0154	4•625	231•2
47.	0•044	0•94	47•0	0•020	0•0018	0•0182	5•187	259•8
48.	0•035	0•75	37•5	0•015	0•00445	0•01055	3•5	175•0
49.	0•048	1•02	51•0	0•017	0•0021	0•0149	4•5	225•0
50.	0•060	1•30	65•0	0•019	0•0029	0•0161	4•75	237•5
51.	0•072	1•55	77•5	0•015	0•0037	0•0113	3•79	184•5
52.	0•082	1•77	88•5	0•020	0•0045	0•0155	4•625	231•2
53.	0•049	1•05	52•5	0•019	0•0022	0•0168	4•875	243•7
54.	0•072	1•55	77•5	0•014	0•0037	0•0103	3•49	174•5
55.	0•033	0•68	34•0	0•022	0•00127	00273	5•75	287•5
56.	0•060	1•30 65 0	65•0	0•025	0•0029	0•0221	6•03	301•5

Table No. XIV.

ESTIMATION OF CAROTENE AND VITAMIN-A IN BLOOD OF NORMAL ADULTS.

FEMALES.

No.	Instrumental Reading for Carotene	Carotene in 2 cc. serum	Carotene in I.U. in 100 cc. serum	Inst. Reading for vit. A	Interference for carotene	True Reading for carotene	Vitamin A in 2 cc. serum	Vitamin A in I.U. in 100 cc. serum
1.	0.060	1.32	66.0	0.010	0.003	0.007	2.800	140.0
2.	0.075	1.62	81.0	0.009	0.0039	0.0051	2.3125	115.6
3.	0.087	1.87	93.5	0.009	0.005	0.004	2.125	106.2
4.	0.090	1.95	97.5	0.015	0.0052	0.0098	3.375	168.7
5.	0.034	1.72	36.0	0.010	0.0043	0.0057	2.500	125.0
6.	0.050	1.75	87.5	0.011	0.0044	0.0066	2.687	134.3
7.	0.073	1.57	78.5	0.015	0.0038	0.0112	3.680	184.0
8.	0.074	1.60	80.0	0.012	0.0039	0.0081	3.000	150.0
9.	0.066	1.42	71.0	0.010	0.0033	0.0067	2.69	134.5
10.	0.054	1.54	77.0	0.020	0.0037	0.0163	4.82	241.0
11.	0.032	0.70	35.0	0.007	0.0013	0.0057	2.50	125.0
12.	0.052	1.10	55.0	0.015	0.0023	0.0127	4.00	200.0
13/								

13.	0.074	1.60	80.0	0.019	0.0039	0.0151	4.50	225.0
14.	0.063	1.25	62.5	0.015	0.0027	0.0123	3.875	193.7
15.	0.051	1.10	55.0	0.020	0.0023	0.0177	5.062	235.1
16.	0.045	0.97	48.5	0.021	0.0019	0.0191	5.375	268.7
17.	0.045	0.97	48.5	0.017	0.0019	0.0151	4.500	225.0
18.	0.070	1.50	75.0	0.015	0.0035	0.0115	3.750	187.5
19.	0.063	1.35	67.5	0.016	0.0031	0.0129	4.03	201.5
20.	0.056	1.20	60.0	0.017	0.0026	0.0144	4.37	218.5
21.	0.043	0.92	46.0	0.017	0.0018	0.0152	4.66	233.0
22.	0.065	1.40	70.0	0.016	0.0031	0.0129	4.03	201.5
23.	0.064	1.37	68.5	0.018	0.0032	0.0148	4.44	202.0
24.	0.060	1.30	65.0	0.019	0.0029	0.0161	4.75	237.5
25.	0.070	1.50	75.0	0.018	0.0035	0.0145	4.37	218.5
26.	0.050	1.10	55.0	0.014	0.0023	0.0117	3.81	190.5
27.	0.048	1.02	51.0	0.012	0.0021	0.0099	3.37	168.5
28/								

28.	0.066	1.42	71.0	0.019	0.0033	0.0157	4.63	231.5
29.	0.035	0.75	37.5	0.016	0.0017	0.0146	4.42	221.0
30.	0.051	1.10	55.0	0.015	0.0023	0.0127	4.00	200.0
31.	0.058	1.25	62.5	0.017	0.0027	0.0143	4.31	215.0
32.	0.035	0.75	37.50	0.016	0.0014	0.0146	4.42	221.0
33.	0.133	2.22	111.0	0.014	0.0062	0.0078	2.87	143.5
34.	0.095	2.05	102.5	0.012	0.0056	0.0064	2.62	131.0
35.	0.059	1.24	62.0	0.011	0.00265	0.00835	3.19	159.5
36.	0.057	1.22	61.0	0.008	0.00260	0.0054	2.38	119.0
37.	0.095	2.05	102.5	0.019	0.0056	0.0134	4.18	209.0
38.	0.076	1.65	82.5	0.014	0.0041	0.0099	3.38	169.0
39.	0.078	1.67	83.5	0.009	0.0042	0.0048	2.25	112.5
40.	0.083	1.80	90.0	0.015	0.0047	0.0103	3.50	175.0
41.	0.073	1.57	78.5	0.011	0.0038	0.0072	2.81	140.5
42/								

42.	0.086	1.85	92.5	0.017	0.0048	0.0122	3.87	193.5
43.	0.085	1.82	91.0	0.010	0.0047	0.0053	2.38	119.0
44.	0.155	3.37	168.5	0.018	0.0122	0.0058	2.50	125.0
45.	0.122	2.37	118.5	0.008	0.007	0.0010	1.44	72.0
46.	0.062	1.32	66.0	0.009	0.003	0.0060	2.53	126.5
47.	0.052	1.10	55.0	0.008	0.0023	0.0057	2.49	124.5
48.	0.064	1.37	68.5	0.008	0.0031	0.0049	2.69	134.5
49.	0.142	3.07	153.5	0.015	0.0104	0.0046	2.23	111.5
50.	0.075	1.62	81.0	0.009	0.004	0.0050	2.31	115.0
51.	0.043	0.92	46.0	0.017	0.0018	0.0152	4.55	227.5
52.	0.056	1.20	60.0	0.014	0.00255	0.0124	3.87	193.5
53.	0.075	1.60	80.0	0.023	0.0039	0.0181	5.19	259.5
54.	0.073	1.56	78.0	0.022	0.0037	0.0183	5.19	259.5
55.	0.053	1.10	55.0	0.010	0.0023	0.0077	2.94	147.0
56/								

56.	0.068	1.48	74.0	0.014	0.00345	0.0105	3.50	175.0
57.	0.031	0.64	32.0	0.006	0.0012	0.0048	2.25	112.5
58.	0.019	0.43	21.5	0.010	0.00075	0.00925	3.25	162.5

Average of 58 females vitamin A being 174 I.U. and carotene being 71 I.U.

" " 56 males " " " 200 I.U. " " " 65 I.U.

Statistically standard deviation in females for vitamin A being ± 48.7 carotene being ± 26.1

" " " " males " " " " ± 48.4 carotene being ± 17.9

Average of 114 normal subjects (Both sexes) Vitamin A - 187 I.U. Carotene - 68 I.U.

Table No. XV.

BLOOD VITAMIN-A AND CAROTENE ESTIMATION IN PATIENTS OF ACNE VULGARIS.

No.	Name	Sex	Age	Occupation	Inst. Read for carot.	Carot. in 2 cc. serum	Carot. in I.U. in 100 cc. serum	Inst. Read for vit. A	Interference for carotene	True Read for vit.A	Vit.A in 2 cc. serum	Vit.A in I.U. in 100 cc. serum
1.	H.L.	F.	24	Typist	0.072	1.55	77.50	0.009	0.0037	0.0053	2.37	118.5
2.	C.G.	F.	19	Civil Servant	0.070	1.50	75.00	0.008	0.0035	0.0045	2.25	112.5
3.	C.N.	F.	14	School Girl	0.036	0.77	38.50	0.011	0.0013	0.0097	3.37	168.5
4.	A.W.	M.	21	Fitter	0.034	0.72	36.00	0.016	0.0014	0.0146	4.43	221.5
5.	N.McD	M.	16	School Boy	0.068	1.47	73.50	0.015	0.0035	0.0115	3.55	177.5
6.	J.McC	M.	15	Restaurant Asst.	0.074	1.60	80.00	0.008	0.0039	0.0041	2.18	109.5
7.	K.P.	F.	21	Clerkess	0.085	1.82	91.00	0.017	0.0047	0.0123	3.93	196.5
8.	J.T.	M.	23	Clerk	0.020	0.45	22.50	0.012	0.0008	0.0112	3.69	184.5
9.	J.I.	M.	18	Printer's Clerk	0.058	1.25	62.50	0.013	0.0027	0.0103	3.50	175.0
10.	C.W.	M.	16	School Boy	0.024	0.50	25.00	0.017	0.0009	0.0161	4.63	231.5
11.	W.M.	M.	18	Laboratory Tech.	0.027	0.57	28.50	0.012	0.0011	0.0109	3.63	181.5
12.	M.McA	F.	20	Clerkess	0.054	1.51	57.50	0.008	0.0024	0.0056	2.47	123.5
13.	J.M.	M.	15	Farm Worker	0.027	0.57	28.50	0.004	0.0011	0.0029	1.88	94.0
14.	D.M.	M.	16	Electrician	0.030	0.520	26.00	0.004	0.0009	0.0031	1.90	95.0

15/

15.	J.C.	M.	23	Clerk	0.080	1.72	86.00	0.012	0.0043	0.0077	3.06	153.0
16.	A.H.	M.	18	University Student	0.077	1.65	82.50	0.015	0.0041	0.0109	3.63	181.5
17.	J.S.	M.	18	School Boy	0.054	1.15	57.50	0.010	0.0024	0.0076	2.87	143.5
18.	J.Y.	M.	18	Miner	0.025	0.60	25.00	0.008	0.0009	0.0071	2.81	140.5
19.	J.I.	M.	19	Plumber	0.058	1.25	62.50	0.013	0.0027	0.0103	3.50	175.0
20.	S.L.	F.	35	Housewife	0.025	0.50	25.00	0.012	0.0009	0.0111	3.69	184.5
21.	I.McD	F.	15	Artist	0.068	1.47	73.50	0.011	0.0034	0.0076	2.87	143.5
22.	P.G.	F.	22	Housewife	0.074	1.60	80.00	0.015	0.0039	0.0110	3.69	184.5
23.	E.K.	M.	17	Construct.	0.030	0.52	26.00	0.012	0.001	0.0111	3.63	181.5
24.	W.C.	M.	20	University Student	0.061	1.33	66.50	0.011	0.003	0.008	3.00	150.0
25.	E.B.	F.	22	Factory Worker	0.035	0.75	37.50	0.010	0.0014	0.0086	3.42	156.0
26.	S.S.	M.	24	Grocer	0.050	1.10	55.00	0.013	0.0023	0.0107	3.57	178.5
27.	J.M.	M.	38	Steel Worker	0.038	0.80	40.00	0.010	0.0015	0.0085	3.10	155.0
28.	W.F.	F.	19	Nurse	0.058	1.25	62.50	0.015	0.0027	0.0123	3.94	197.0
29.	R.R.	M.	18	Engineer	0.055	1.17	58.00	0.012	0.0025	0.0095	3.31	165.5

30/

30.	I.P.	F.	28	Clerkess	0.076	1.65	82.50	0.013	0.0041	0.0089	3.23	161.5
31.	C.C.	F.	17	School Girl	0.033	0.72	36.00	0.012	0.0014	0.0106	3.56	178.0
32.	A.McP	F.	20	Clerkess	0.046	1.00	50.00	0.008	0.0020	0.0060	2.56	128.0
33.	T.B.	F.	23	School Teacher	0.096	2.07	103.50	0.013	0.0057	0.0073	2.81	140.5
34.	J.H.	F.	16	Clerkess	0.052	1.12	56.00	0.012	0.0024	0.0096	3.31	165.5
35.	M.L.	F.	18	Typist	0.055	1.17	58.50	0.013	0.0025	0.0105	3.55	177.5
36.	H.T.B.M.		21	University Student	0.050	1.10	55.00	0.008	0.0023	0.0101	3.43	171.5
37.	G.Q.	M.	25	Accountant	0.074	1.60	80.00	0.014	0.0039	0.0101	3.43	171.5
38.	A.AcG.	F.	15	School Girl	0.035	0.75	37.50	0.010	0.0014	0.0086	3.12	156.0
39.	M.P.	F.	22	Book Binder	0.055	1.17	58.50	0.013	0.0025	0.0105	3.55	177.5
40.	E.T.	F.	21	Civil Servant	0.027	0.57	28.50	0.012	0.0011	0.0109	3.20	160.0
41.	J.M.	F.	17	School Girl	0.068	1.47	73.50	0.015	0.0034	0.0116	3.78	189.0
42.	J.F.	F.	19	Clerkess	0.097	2.08	104.00	0.014	0.006	0.008	3.00	150.0
43.	A.S.	M.	21	Coal Porter	0.050	1.10	55.00	0.013	0.0023	0.0107	3.57	178.5
44.	L.W.	M.	15	School Boy	0.074	1.60	80.00	0.009	0.0039	0.0051	2.63	131.5

45/

45.	E.Y.	F.	21	Typist	0.060	1.30	65.00	0.007	0.0029	0.0041	2.19	109.5
46.	J.R.	M.	22	University Student	0.070	1.50	79.00	0.005	0.0038	0.0120	3.88	194.0
47.	M.M.	F.	16	Shop Asst.	0.070	1.50	75.00	0.010	0.0035	0.0065	2.65	132.5
48.	M.B.	F.	23	Clerkess	0.046	0.95	49.00	0.014	0.0019	0.0121	3.89	194.5
49.	J.C.	F.	15	School Girl	0.074	1.60	80.00	0.012	0.0039	0.0081	3.02	151.0
50.	T.M.	M.	28	Labourer	0.028	0.51	25.50	0.007	0.0009	0.0061	2.59	129.5
51.	M.B.	F.	20	Clerkess	0.058	1.25	62.50	0.020	0.0027	0.0173	5.00	250.0
52.	M.S.	F.	28	Unemployed	0.068	1.47	73.5	0.011	0.0035	0.0075	2.75	137.5
53.	N.O.	M.	14	School Boy	0.090	1.95	97.5	0.021	0.0053	0.0157	4.65	232.5
54.	J.T.	F.	23	Civil Serv.	0.072	1.55	77.5	0.012	0.0037	0.0083	3.06	153.0
55.	J.F.	F.	19	University Student	0.049	1.05	52.50	0.010	0.0022	0.0078	2.94	147.0
56.	J.M.	F.	19	Maid	0.026	0.55	27.50	0.009	0.0010	0.0080	3.00	150.0
57.	E.W.	F.	16	Clerkess	0.051	1.15	57.5	0.024	0.0024	0.0216	5.90	295.0
58.	M.T.	M.	22	Clerk	0.071	1.50	75.0	0.020	0.0035	0.0165	4.80	240.0
59.	G.L.	M.	12	School Boy	0.035	0.75	37.50	0.011	0.0014	0.0096	3.31	165.0

60/

60.	J.F.	M.	18	Baker	0•062	1•36	68•0	0•011	0•0031	0•0089	3•23	161•5
61.	M.S.	F.	26	Bank Clerkess	0•037	0•80	40•0	0•016	0•0043	0•0127	4•03	201•5
62.	S.M.	F.	12	School Girl	0•090	1•95	97•50	0•016	0•0053	0•0107	3•55	177•5
63.	C.E.	F.	14	School Girl	0•033	0•72	36•00	0•010	0•0014	0•0086	3•12	156•0
64.	W.Y	M.	21	Joiner	0•080	1•72	86•00	0•015	0•004	0•0110	3•63	181•5
65.	J.L.	M.	19	Laboratory Tech.	0•050	1•10	55•00	0•030	0•0023	0•0277	7•24	362•0
66.	A.B.	M.	21	Fireman	0•046	1•00	50•00	0•010	0•0020	0•008	3•00	150•0
67.	G.McD	M.	21	Labourer	0•073	1•57	78•50	0•013	0•0038	0•0102	3•46	173•0
68.	J.F.	M.	18	Baker	0•061	1•32	66•00	0•021	0•0029	0•0181	5•18	259•0
69.	L.W.	M.	15	School Boy	0•063	1•35	67•50	0•030	0•0031	0•0269	7•05	352•5
70.	T.S.	M.	16	Electrician	0•055	1•17	58•50	0•011	0•0025	0•0085	3•10	155•0
71.	E.C.	M.	20	University Student	0•044	0•95	47•50	0•019	0•0019	0•0171	4•93	246•5
72.	S.McL	F.	22	Clerkess	0•073	1•57	78•50	0•009	0•0080	0•0010	1•50	75•0
73.	J.F.	M.	18	Baker	0•030	0•52	26•00	0•015	0•0010	0•0140	4•31	215•0
74.	E.McB	F.	26	Housewife	0•096	2•05	102•50	0•008	0•0050	0•0240	6•50	325•0
75.	C.W.	M.	16	School Boy	0•044	0•95	47•50	0•014	0•0019	0•0121	3•89	194•5

Table No. XVI.

BLOOD VITAMIN-A AND CAROTENE ESTIMATION IN PATIENT.

(ICHTHYOSIS)

No.	Name	Sex	Age	Occupation	Inst. Read for carot.	Carot. in 2 cc. serum	Carot. in I.U. in 100 cc. serum	Inst. Read for vit. A	Interference for carot.	True Read for vit.A	Vit. A in 2 cc. serum	Vit. A in I.U. in 100 cc. serum
1.	J.B.	M.	14	School Boy	0.072	1.55	77.5	0.008	0.0038	0.0042	2.18	109.0
2.	J.D.M	M.	43	Musician	0.085	1.82	91.0	0.009	0.0047	0.0043	2.20	110.0
3.	J.M.	M.	75	Painter	0.090	1.95	97.5	0.010	0.0053	0.0047	2.25	112.5
4.	I.R.	F.	27	Housewife	0.057	1.22	61.0	0.013	0.0026	0.0104	3.50	175.0
5.	A.R.	M.	50	Postman	0.060	1.30	65.0	0.010	0.0029	0.0071	3.81	190.5
6.	N.P.	F.	29	Private Secretary	0.070	1.50	75.0	0.008	0.0035	0.0045	2.25	112.5
7.	F.T.	M.	27	Unemployed	0.045	0.97	48.5	0.006	0.0019	0.0041	2.19	109.5
8.	H.S.	F.	21	Serving Maid	0.057	1.22	61.0	0.007	0.0026	0.0044	2.23	111.5
9.	J.B.	M.	18	Labourer	0.047	1.02	51.0	0.010	0.0021	0.0079	3.00	150.0
							mean 73 3					mean 131

Table No. XVLL.

BLOOD VITAMIN-A AND CAROTENE ESTIMATION IN PATIENT

(PITYRIASIS RUBRA PILARIS)

No.	Name	Sex	Age	Occupation	Inst. Read for carot.	Carot. in 2 cc. serum	Carot. in I.U. in 100 cc. serum	Inst. Read for vit.A	Interference for carotene	True Read for vit.A	Vit. A in 2 cc. serum	Vit.A in I.U. in 100 cc serum
1.	B.MacM	F.	44	Housewife	0.029	0.51	25.0	0.003	0.0009	0.0021	1.69	84.5
	½ month after injection				0.028	0.48	24.0	0.003	0.0010	0.0020	1.60	80.0
	After one month				0.069	1.48	74.0	0.009	0.0034	0.0056	2.38	119.0
	After two months				0.074	1.60	80.0	0.010	0.0039	0.0061	2.44	122.0
	After three months				0.050	1.10	55.0	0.016	0.0023	0.0137	4.19	209.5
	After four months				0.055	1.17	58.5	0.017	0.0025	0.0145	4.40	220.0
	After five months				0.054	1.15	57.5	0.014	0.0024	0.0116	3.81	190.5

Table No. XVIII.

BLOOD VITAMIN-A AND CAROTENE ESTIMATION IN PATIENT.

(NUMMULAR ECZEMA).

No.	Name	Sex	Age	Occupation	Inst. Read for carot.	Carot. in 2 cc. serum	Carot. in I.U. in 100 cc. serum	Inst. Read for vit. A	Interference for carot.	True Read for vit.A	Vit. A in 2 cc. serum	Vit. A in I.U. in 100 cc. serum
1.	A.P.	M.	13	School Boy	0•030	0•52	26•00	0•010	0•00095	0•0091	3•25	162•5
2.	D.S.	M.	41	Cashier	0•050	1•10	55•00	0•014	0•0023	0•0117	3•81	190•5
3.	A.A.	F	21	Dairy Maid	0•080	1•72	86•00	0•010	0•0043	0•0057	2•50	125•0
4.	J.McL	M.	53	Foreman	0•060	1•30	65•00	0•017	0•0029	0•0141	4•43	221•5
5.	A.McG	F.	44	Housewife	0•076	1•65	82•50	0•009	0•0041	0•0049	2•31	115•0
6.	W.D.	M.	42	Hammerman	0•047	1•02	51•00	0•012	0•0022	0•0099	3•37	168•0
7.	G.C.	M.	60	Shipbuilder	0•035	0•75	37•50	0•015	0•0014	0•0136	4•18	209•0
8.	C.B.	F.	30	Dairy Worker	0•062	1•32	66•00	0•007	0•0032	0•0038	2•05	102•5
9.	M.L.	F.	27	Housewife	0•061	1•31	65•00	0•011	0•0031	0•0079	2•93	146•5
10.	T.T.	M.	41	Brewery Worker	0•090	1•95	97•50	0•013	0•0053	0•0077	2•90	145•0
11.	E.F.	F.	22	Med. Student	0•036	0•77	38•50	0•016	0•0015	0•0145	4•37	218•5
12.	A.D.	F.	21	Med. Student	0•063	1•36	68•00	0•014	0•0032	0•0108	3•56	178•0
13.	C.McC	M.	36	Clerk	0•070	1•50	75•00	0•012	0•0036	0•0084	3•06	153•0

14/

14.	C.G.	M.	28	Labourer	0•030	0•52	26•00	0•004	0•0009	0•0031	1•93	96•5
15.	L.W.	F.	26	Housewife	0•074	1•60	80•00	0•009	0•0039	0•0051	2•37	118•5
16.												

Table No. XIX.

BLOOD VITAMIN-A AND CAROTENE ESTIMATION IN PATIENT.

(BESNIER'S PRURIGO).

No.	Name	Sex	Age	Occupation	Inst. Read for carot.	Carot. in 2 cc serum	Carot. in I.U. in 100 cc serum	Inst. Read for vit. A	Interference for carot.	True Read for vit.A	Vit. A in 2 cc serum	Vit. A in I.U. in 100 cc. serum
1.	R.M.	M.	25	Art Sale.	0.055	1.77	58.50	0.025	0.0027	0.0223	6.06	303.0
2.	H.S.	F.	21	Serving Maid	0.049	1.05	52.50	0.012	0.0022	0.0098	3.37	168.5
3.	T.McA	M.	25	Clerk	0.070	1.50	75.00	0.010	0.0036	0.0064	2.62	131.0
4.	I.H.	F.	24	Clerkess	0.061	1.32	66.00	0.011	0.0029	0.0081	5.18	259.0
5.	M.L.	F.	26	Housewife	0.044	0.95	47.50	0.020	0.0019	0.0181	3.25	162.5
6.	J.H.	M.	27	Motor Driver	0.050	1.10	55.00	0.022	0.0023	0.0197	5.50	275.0
7.	R.O.	M.	13	School Boy	0.070	1.50	75.00	0.021	0.0036	0.0174	5.00	250.0
8.	J.S.	F.	12	School Boy	0.044	0.95	47.50	0.014	0.0019	0.0121	3.93	196.5
9.	J.G.	F.	33	Housewife	0.035	0.75	37.50	0.010	0.0014	0.0086	3.12	156.0
10.	E.F.	F.	45	Factory Worker	0.052	1.12	56.00	0.009	0.0024	0.0066	2.16	108.0
11.	M.B.	F.	15	School Girl	0.053	1.15	57.00	0.009	0.0024	0.0066	2.16	108.0
12.	H.H.	M.	16	Clerk	0.050	1.10	55.00	0.013	0.0023	0.0107	3.56	178.0
13.	W.I.	F.	20	Clerkess	0.073	1.57	78.50	0.019	0.0038	0.0152	4.55	227.5

14.	G.M.	M.	17	Worker	0.042	0.90	45.00	0.013	0.0018	0.0112	3.82	191.0
15.	R.M.	M.	22	Clerk	0.026	0.55	27.50	0.015	0.0010	0.0140	4.31	215.5
16.	I.S.	F.	17	Maid	0.063	1.35	67.50	0.016	0.0031	0.0129	4.86	203.0
							56 I.U.				mean	195.7

Table No. XX.

BLOOD CAROTENE AND VITAMIN ESTIMATION IN PATIENTS.

(NEURODERMATITIS)

No.	Name	Sex	Age	Occupation	Inst. Read for carot.	Carot. in 2 cc serum	Carot. in I.U. in 100 cc. serum	Inst. Read for vit.A	Interference for carot.	True Read for vit.A	Vit. A in 2 cc serum	Vit. A in I.U. in 100 cc serum
1.	P.W.	M.	38	Miner	0.074	1.60	80.0	0.009	0.0039	0.0051	2.37	118.0
2.	I.F.	F.	40	Housewife	0.027	0.51	25.0	0.015	0.009	0.0060	2.56	128.0
3.	M.L.	F.	36	Housewife	0.034	0.72	36.0	0.017	0.0014	0.0156	4.63	231.5
4.	L.N.	M.	46	Tram Driver	0.038	0.80	45.0	0.015	0.0015	0.0135	4.19	204.5
5.	E.S.	F.	41	Housewife	0.036	0.77	38.5	0.014	0.0015	0.0125	4.03	201.5
6.	J.G.	F.	49	Housewife	0.075	1.62	81.2	0.020	0.0040	0.0160	4.73	236.5
7.	R.S.	M.	62	Labourer	0.035	0.75	37.5	0.015	0.0014	0.0136	4.20	210.0
							mean 49					mean 190

Table No. XXI.

BLOOD VITAMIN-A AND CAROTENE ESTIMATION IN PATIENTS.

(ALOPECIA AREATA)

No.	Name	Sex	Age	Occupation	Inst. Read for carot.	Carot. in 2 cc serum	Carot. in I.U. in 100 cc serum	Inst. Read for vit. A	Interference for carotene	True Read for vit.A	Vit. A in 2 cc serum	Vit. A in I.U. in 100 cc serum
1.	E.McD	F.	27	Shop Asst.	0.072	1.55	77.5	0.014	0.0037	0.0103	3.50	175.0
2.	A.W.	M.	36	Housewife	0.030	0.52	26.0	0.013	0.0009	0.0121	3.88	194.0
3.	A.C.	F.	37	Shop Asst.	0.050	1.10	55.0	0.013	0.0023	0.0107	3.63	181.5
4.	A.L.	M.	18	Unemployed	0.042	0.82	46.0	0.015	0.0016	0.0134	4.14	207.0
5.	B.S.	F.	33	Housewife	0.080	1.82	91.0	0.014	0.0047	0.0093	3.25	162.5
6.	T.C.	M.	60	Baker	0.085	1.82	91.0	0.014	0.0047	0.0093	3.25	162.5
7.	T.G.	F.	42	Housewife	0.078	1.67	83.5	0.012	0.0042	0.0078	2.92	146.0
(P.P. de Broq.)						mean	67					175.4

Table No. XXII

BLOOD CAROTENE AND VITAMIN-A ESTIMATION IN PATIENTS.
(LUPUS ERYTHEMATOSUS DESCOID TYPE).

No.	Name	Sex	Age	Occupation	Inst. Read for carot.	Carot. in 2 cc serum	Carot. in I.U. in 100 cc. serum	Inst. Read for vit. A	Interference for carotene	True Read for vit.A	Vit. A in 2 cc serum	Vit. A in I.U. in 100 cc serum
1.	E.P.	F.	30	Housewife	0.076	1.65	82.5	0.016	0.0041	0.0119	3.87	193.5
2.	J.G.	F.	37	Weaver	0.054	1.15	57.5	0.017	0.0024	0.0146	4.40	220.0
3.	M.R.	F.	57	Housewife	0.072	1.55	77.5	0.022	0.0037	0.0183	5.20	260.0
4.	E.J.	F.	68	Housewife	0.020	0.42	21½	0.008	0.0007	0.0073	2.81	140.5
5.	I.L.	F.	28	Clerkess	0.028	0.55	27.5	0.013	0.0010	0.0120	3.87	193.5
6.	A.S.	M.	36	Eng. Driver	0.046	0.97	48.7	0.020	0.0019	0.0181	5.16	258.0
						mean	38.7				mean	210

Table No. XXIII.

BLOOD VITAMIN-A AND CAROTENE ESTIMATION IN PATIENTS.
(KERATODERMA PALMARIS ET PLANTARIS).

1.	M.A.	F.	60	Housewife	0.052	1.12	56.00	0.010	0.0024	0.0076	2.87	143.5
2.	A.R.	M.	45	Labourer	0.071	1.50	75.00	0.024	0.0036	0.0204	5.62	281.0
							mean 65					mean 212

Table No. XXIV.

BLOOD VITAMIN-A AND CAROTENE ESTIMATION IN PATIENTS.
(LICHEN PLANUS).

No.	Name	Sex	Age	Occupation	Inst. Read for carot.	Carot. in 2 cc serum	Carot. in I.U. in 100 cc serum	Inst. Read for vit. A	Interference for vit. A	True Read for vit. A	Vit. A in 2 cc serum	Vit. A in I.U. in 100 cc serum
1.	M.H.	F.	56	Housewife	0.046	1.00	50.0	0.019	0.002	0.0170	4.94	247.0
2.	K.G.	F.	72	Housewife	0.0118	2.55	127.5	0.026	0.0077	0.0183	5.25	262.5
3.	W.B.	F.	58	Housewife	0.065	1.40	70.0	0.028	0.0032	0.0248	6.62	331.0
4.	E.M.	F.	41	Housewife	0.064	1.37	68.5	0.026	0.0077	0.0183	5.25	262.5
5.	G.S.	M.	36	Miner	0.125	2.70	135.0	0.032	0.0084	0.0236	6.37	318.5
6.	A.L.	M.	35	Engineer	0.075	1.62	81.0	0.019	0.0040	0.0150	4.51	225.5
7.	M.H.	F.	58	Shop Asst.	0.055	1.17	58.5	0.018	0.0027	0.0153	4.62	231.0
8.	E.C.	F.	55	Housewife	0.127	2.75	137.5	0.030	0.0087	0.0213	5.80	290.0
9.	J.D.	F.	71	Housewife	0.074	1.60	80.0	0.020	0.0039	0.0161	4.75	237.5
10.	E.M.	F.	40	Housewife	0.138	3.00	150.0	0.025	0.0100	0.0240	6.43	321.5
11.	G.D.	M.	56	Manager Dana Hall	0.146	3.15	157.5	0.025	0.0180	0.0070	2.78	139.0
12.	B.D.	F.	27	Housewife	0.0160	3.47	173.5	0.019	0.0125	0.0065	2.68	134.0
13.	R.W.	M.	49	Hair Dresser	0.090	1.95	92.5	0.022	0.0052	0.0168	4.87	243.5
14.	J.G.	F.	49	Housewife	0.056	1.30	60.0	0.025	0.0026	0.0224	6.07	303.5
15.	E.B.	F.	52	Housewife	0.081	1.73	86.5	0.021	0.0043	0.0167	4.85	242.5
						mean	81.2				mean	252.6

Table No. XXV.

BLOOD VITAMIN-A AND CAROTENE IN PATIENTS.

(PSORIASIS).

No.	Name	Sex	Age	Occupation	Inst. Read for carot.	Carot. in I.U. in 100 cc serum	Inst. Read for vit. A	Inst. Read for vit. A	Interference for carotene	True Read for vit. A	Vit. A in 2 cc serum	Vit. A in I.U. 100 cc serum
1.	J.D.	F.	40	Housewife	0.043	0.93	46.0	0.014	0.0018	0.0123	3.93	196.5
2.	E.C	F.	43	Housewife	0.067	1.45	72.5	0.016	0.0034	0.0126	4.00	200.0
3.	J.C.	F.	36	Housewife	0.050	1.10	55.0	0.015	0.0023	0.0127	4.02	210.0
4.	R.H.	M.	34	Bar-man	0.038	0.82	41.0	0.015	0.0016	0.0134	4.19	204.5
5.	I.P.	F.	25	Housewife	0.076	1.65	82.5	0.019	0.0041	0.0149	4.50	225.0
6.	M.M.	F.	33	Housewife	0.056	1.20	60.0	0.028	0.0026	0.0254	6.75	337.5
7.	A.S.	F.	35	Domestic Help	0.055	1.17	58.5	0.025	0.0025	0.0225	6.12	306.0
8.	J.S.	M.	56	Telephone Linesman	0.082	1.75	87.5	0.022	0.0044	0.0176	5.06	253.0
9.	W.B.	M.	21	Med. Student	0.044	0.95	47.5	0.018	0.0019	0.0161	4.75	237.5
10.	A.G.	M.	38	Painter	0.075	1.62	81.0	0.019	0.0040	0.0150	4.50	225.0
11.	M.F.	F.	30	Housewife	0.071	1.52	76.0	0.017	0.0036	0.0177	5.06	253.0
12.	H.W.	F.	24	Housewife	0.071	1.52	76.0	0.017	0.0036	0.0134	4.19	209.5
13.	J.R.	F.	58	Housewife	0.045	0.97	48.5	0.021	0.0019	0.0191	5.37	268.5
14.	H.A.	F.	47	Housewife	0.150	3.25	162.5	0.023	0.0114	0.0116	3.87	193.5
15.	E.H.	M.	32	Clerk	0.050	1.10	55.0	0.012	0.0023	0.0097	3.37	168.5
16.	C.W.	F.	30	Exam. in Books	0.042	0.90	45.0	0.016	0.0017	0.0143	4.37	218.5
17.	M.D.	F.	23	Textile Worker	0.052	1.12	56.0	0.016	0.0024	0.0136	4.62	231.0
							57.5					233.7

VITAMIN-A CLEARANCE TEST.

This test has been done by collecting venous blood in the morning and immediately giving the human adult subject 100,000 int. unit of vitamin A by month or by injection and collecting the blood every 2 hours up to the end of 8 hours and then at 24 hours and at 32 hours.

This clearance test has been done in a normal subject by oral administration as well as by intramuscular injection after an interval of one week (Table No. XXVI - page 104) and shown by a curve (Fig.No.9 - page 106).

This clearance test has been done in a patient of acne vulgaris by oral administration only of vitamin A (Table No. XXVII - page 105) and is shown by curve which has been compared with a clearance curve in a normal human subject (Fig. No. II - page 107).

The vitamin A clearance test has been done in a mixed group of six normal adult human subjects (Table No. XXVIII - page 108) and also in six acne vulgaris patients (Table No. XXIX - page 109). The comparison by curves of normal human subjects with sex acne vulgaris patients have been shown (Fig. No. 12 - page 110).

The vitamin A clearance test has been done in an acne vulgaris patient before starting treatment and again after completion of 3 months treatment (Table NO. XXX - page 109) and has also been shown by a different curves (Fig. No. 16 - page 117).

Estimation/

Table No. XXVI.

VITAMIN-A CLEARANCE TEST IN NORMAL HUMAN SUBJECT.

(AFTER ORAL ADMINISTRATION).

No. Name	Sex	Age	Occp.	Inst. Read for carot.	Carot. in ug in 2 cc serum	Carot. in ug in 100 cc serum	Inst Read for vit.A	Interference for carotene	True Read for vit.A	Vit.A in I.U. in 2 cc serum	Vit.in I.U. in 100 cc ser.	Time
1. J.T.	M.	23	Clerk	0.057	1.22	61.0	0.023	0.0024	0.0206	5.69	284.4	Before Vit.A
				0.062	1.32	66.0	0.024	0.0026	0.0214	5.89	293.5	2 hrs after
				0.055	1.17	58.5	0.062	0.0023	0.0597	15.00	750.0	4 hrs "
				0.062	1.32	66.0	0.081	0.0025	0.0784	17.50	875.0	6 hrs "
				0.035	0.75	37.5	0.024	0.0015	0.0225	12.25	612.5	8 hrs "
				0.060	1.30	65.0	0.024	0.0026	0.0214	5.87	293.5	24 hrs "
				0.057	1.22	61.0	0.023	0.0024	0.0216	5.80	290.0	32 hrs "
Same case	M.	23	Clerk	AFTER INTRMUSCULAR INJECTION								
7 days after				0.062	1.32	66.0	0.024	0.0026	0.0210	5.80	290.0	Before Vit.A
				0.054	1.15	57.5	0.023	0.0023	0.0207	5.70	285.0	2 hrs after
				0.030	0.65	37.5	0.013	0.0013	0.0117	7.62	381.0	4 hrs "
				0.037	0.80	40.0	0.014	0.0016	0.0124	7.86	393.0	6 hrs "
				0.040	0.86	43.0	0.012	0.0017	0.0103	7.00	350.0	8 hrs "
				0.060	1.30	65.0	0.022	0.0026	0.0194	5.44	292.0	24 hrs "
				0.061	1.32	66.0	0.024	0.0026	0.0210	5.80	290.0	32 hrs "

Table No. XXVII.

VITAMIN-A CLEARANCE TEST IN A CASE OF ACNE VULGARIS.

No.	Name	Sex	Age	Occp.	Inst Read for carot.	Carotene in ug in 2 cc serum	Carot. in ug in 100 cc serum	Inst. Read for vit.A	Interference for carotene	True Reading for vit. A	Vit.A in I.U. in 2 cc serum	Vit.A in IU in 100cc ser.	Time
1.	E.W.	F.	16	Clerkess	0•067	1•45	72•5	0•024	0•0029	0•0211	5•800	290•0	Before Vit.A
					0•065	1•40	70•0	0•036	0•0028	0•0332	8•437	421•8	2hrs after
					0•062	1•32	66•0	0•030	0•0027	0•0273	9•000	450•0	4hrs "
					0•064	1•37	68•5	0•046	0•0022	0•0438	10•625	531•2	6hrs "
					0•064	1•37	68•5	0•038	0•0027	0•0353	8•875	443•7	8hrs "
					0•60	1•30	65•0	0•027	0•0026	0•0244	6•500	325•0	24hrs "
					0•66	1•42	71•0	0•025	0•0028	0•0222	6•00	300•0	32hrs "

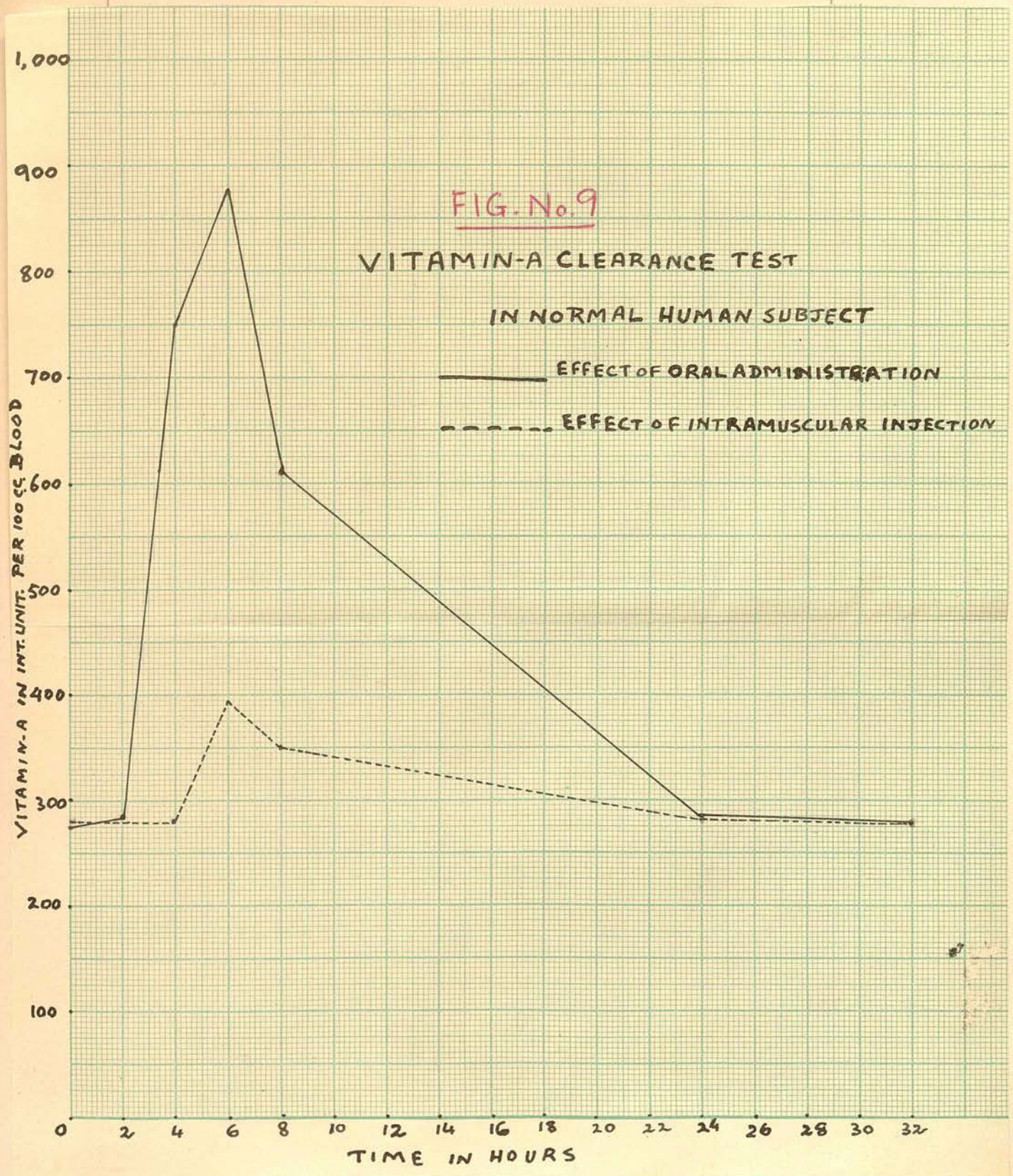


Fig. No. 9 Comparison of vitamen A clearance Test after oral and parenteral adumbrant of vitamen A in a normal subject at interval of one week.

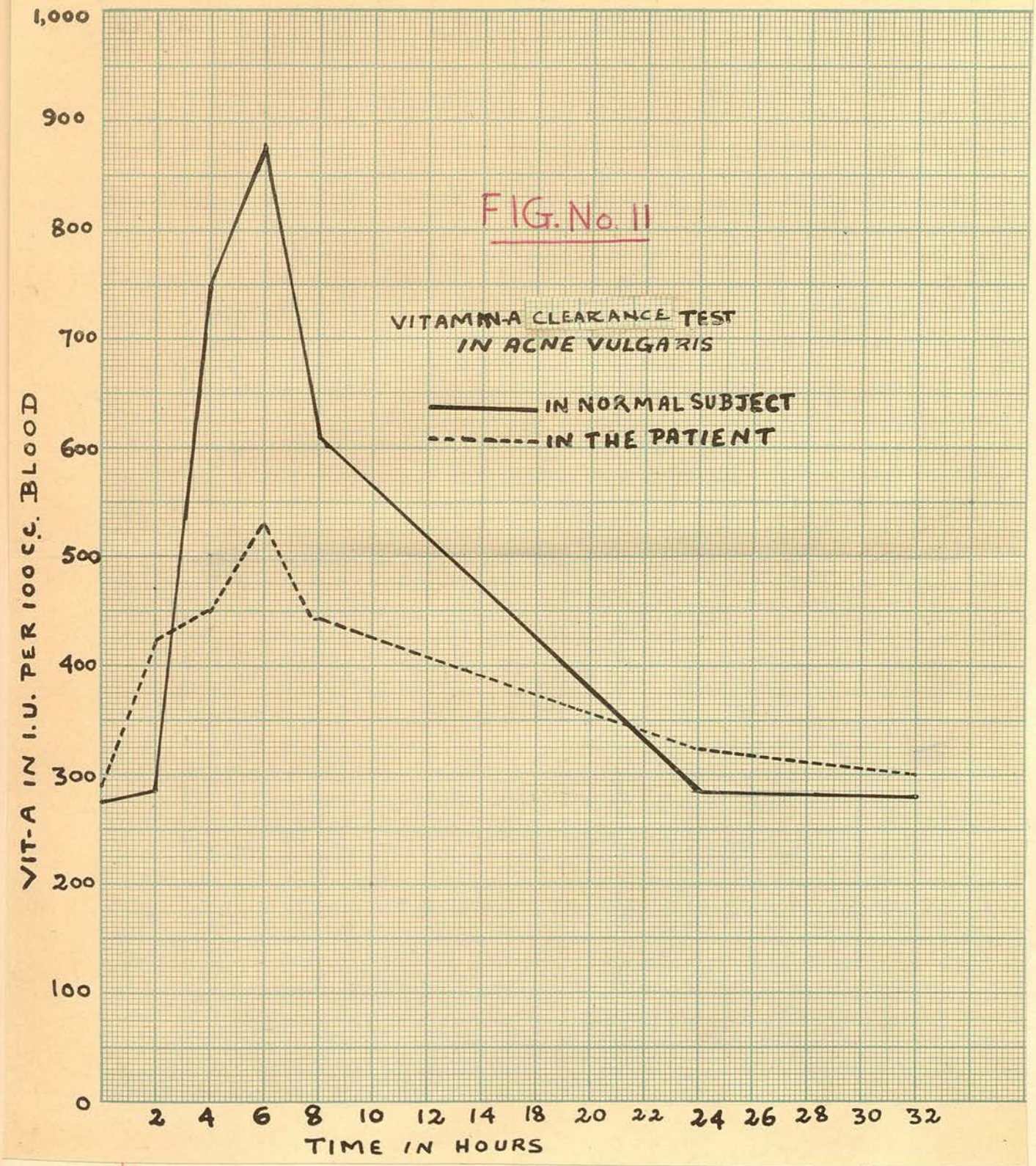


Fig. No. 11 Vitamen A clearance test of a patient of acne vulgaris (shown by dotted lines) compared with the clearance test in a normal subject (shown by plain line).

Table No. XXVIII.

Vitamin A clearance test in six normal adult human males with 100,000 I.U. of vitamin A administered orally.

No.	Name	Age	Sex	Vitamin A in I.U. in blood estimated every 2 hours.						
				'0' hours	2 hours	4hhours	6 hours	8 hours	24 hours	32 hours
1.	R.H.	24	M.	271.4	290.4	720.0	900.0	580.4	274.2	268.8
2.	M.B.	20	F.	287.0	279.8	710.0	830.6	696.2	292.4	284.6
3.	E.P.	22	F.	296.2	300.4	802.0	892.4	718.5	310.2	300.4
4.	P.G.	24	F.	282.4	287.7	742.0	908.2	682.1	288.4	283.1
5.	P.S.	22	M.	283.5	265.5	708.0	841.4	700.1	272.6	271.8
6.	H.G.	21	M.	280.4	307.8	784.4	860.4	648.4	292.6	288.4

Table No. XXIX.

Vitamin A clearance test in six cases of Acne Vulgaris with 100,000 I.U. of vitamin A orally.

No.	Name	Sex	Age	Vitamin A in I.U. in blood estimated every 2 hours						
				'0' hour	2 hours	4 hours	6 hours	8 hours	24 hours	32 hours
1.	E.W.	F.	16	290•0	421•8	450•0	531•2	443•7	325•0	300•0
2.	A.McQ.	M.	22	309•4	500•2	502•6	550•4	508•4	462•7	400•1
3.	A.W.	M.	19	187•8	363•8	390•4	418•7	352•2	338•2	288•4
4.	J.McC.	M.	25	317•2	380•4	392•3	439•2	382•6	360•0	318•2
5.	R.B.	M.	21	260•5	520•3	538•2	552•1	518•4	470•5	420•7
6.	E.H.	M.	19	300•5	448•2	462•2	480•7	438•4	388•2	342•8

Table No. XXX.

Showing difference in clearance tests before and after vitamin A therapy in one Acne Vulgaris patient.

	'0' hour	2 hours	4 hours	6 hours	8 hours	24 hours	32 hours
Before Treatment	192•0	190•0	250•0	310•4	280•0	218•2	210•2
After Treatment	200•4	210•2	325•8	580•8	360•0	235•0	205•0

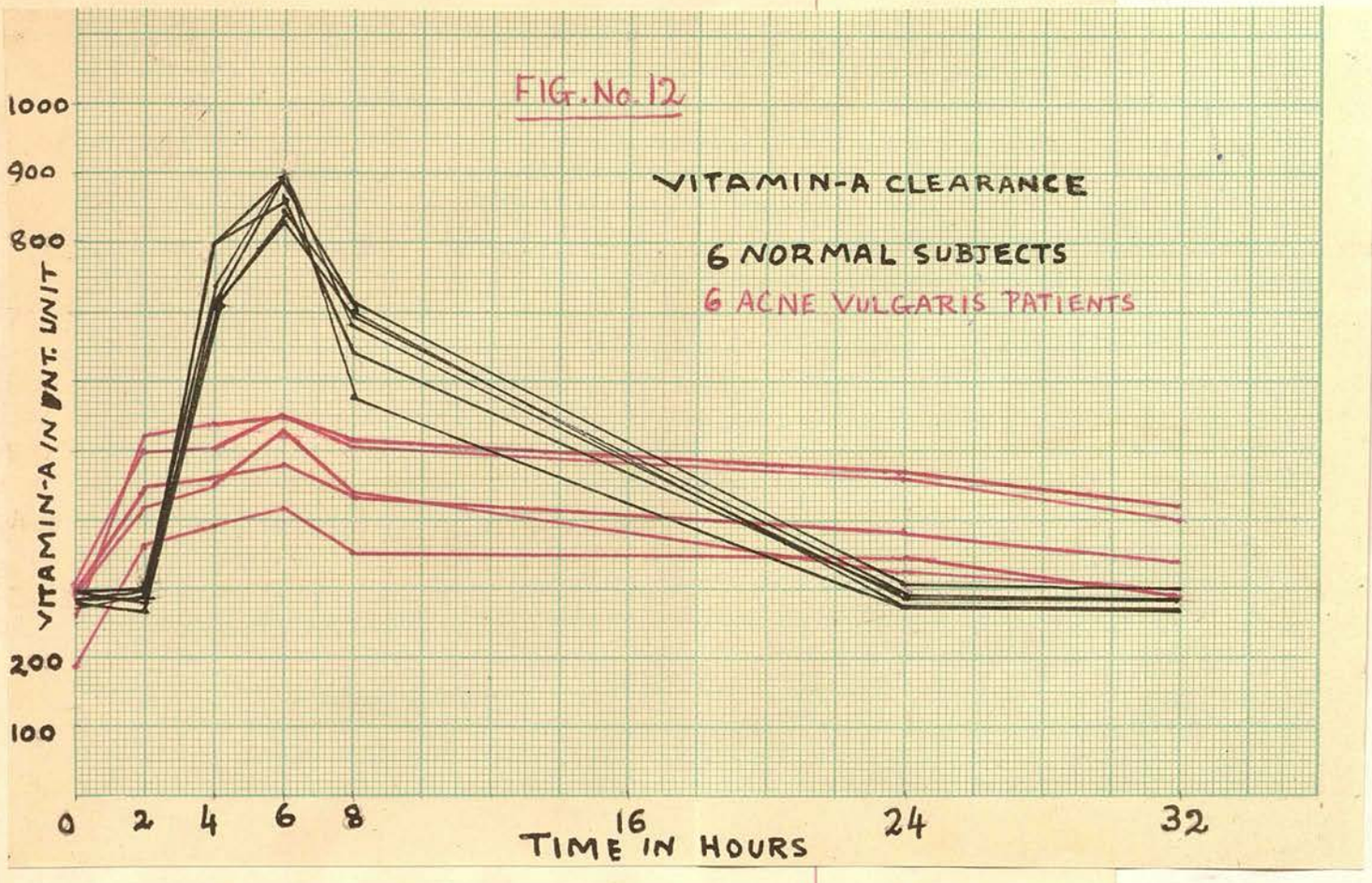


Fig. No. 12. Comparative studies in clearance tests by separate curves for 6 normal subjects (in black ink) as compared with six patients (in red ink).

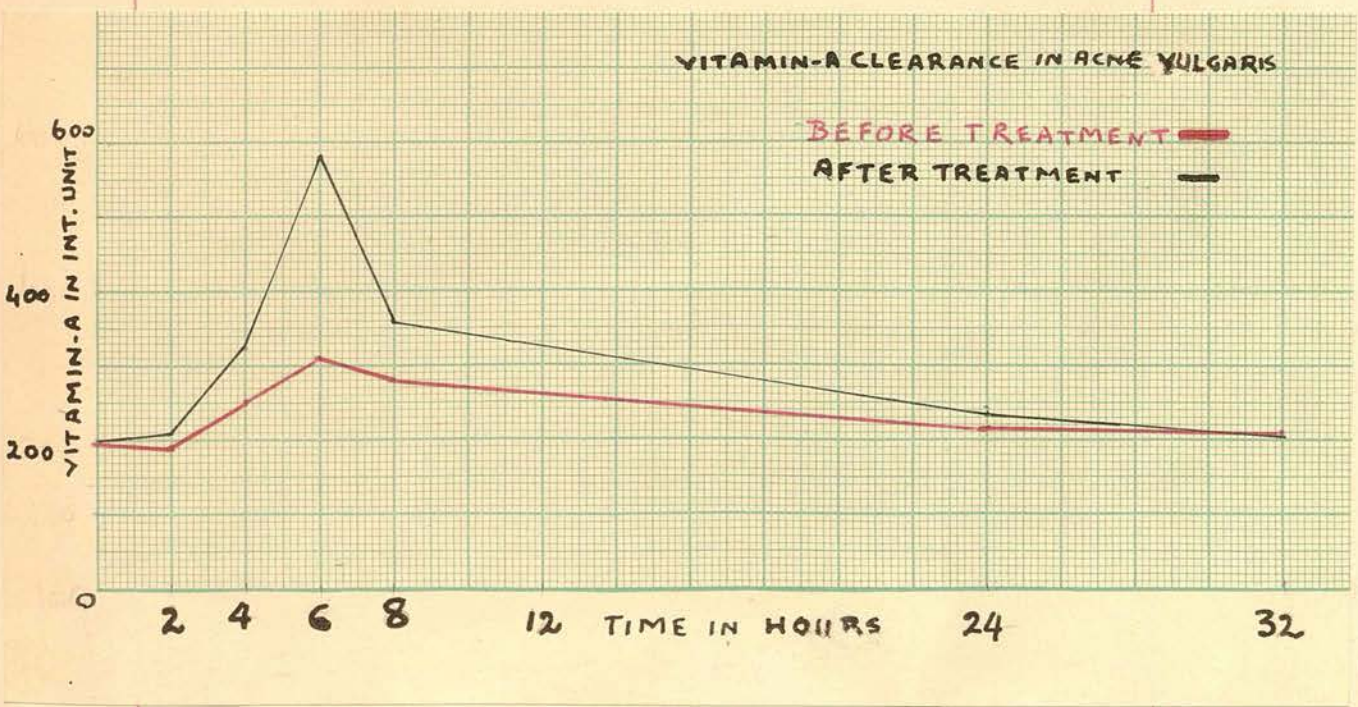


Fig. No. 16. Comparative study of clearance tests in a patient of Acne vulgaris before treatment (as indicated by red line) after treatment (as indicated by black line).

ANDROGEN ESTIMATION IN URINE.

Since there is evidence of influence of some of the hormones, and particularly androgins, in the production of certain skin conditions the estimation of androgins has been done in 24 hours urine in some of the skin diseases.

COLLECTION OF URINE FOR EXPERIMENT:

The first specimen of urine passed on the first morning of the first day of collection is discarded and then all the urine passed up to and including the first morning specimen on the second day is collected. Preservations are not used (copper sulphate may be added to inhibit urease activity and preservations of the phenolic and crissolic type should not be used).

REAGENTS: (1) Absolute alcohol (2) m-dinitrobenzene (DNB). The purified compound does not keep very well although it is protected from light and air. Hence a 2 per cent W/v solution is prepared and preserved in a dark bottle with a glass stopper and the solution is stable for 2 weeks (3) Potassium hydroxide 2·5 N in absolute alcohol is prepared and used freshly prepared.

METHOD FOR ESTIMATION OF 17 KETOSTEROIDS IN URINE:

100 cc. of urine is taken in a conical flask and 10 cc. of cone. Hydrochloric and added and the solution is brought to the boil under a reflex condenser and then boiled for 10 minutes. Burner is removed and the solution is allowed to cool down till it is just bearable to the hand. 30 cc. of carbon tetrachloride is/

is poured down the dondenser and the burner is again applied to the flask and is brought to the boil and maintained then for 10 minutes. When cooled down to room temperature is poured in a separating funnel.

The carbon tetrachloride layer is separated, 10cc. of fresh carbon tetrachloride is added and mixed by swirling and again separated. Carbon tetrachloride extracted is 50 cc. which is washed with (1) 20 cc of water (2) 20 cc of 2N sodium Hydroxide (3) 20 cc of water and (4) 20 cc of water. Washed extract evaporated to dozners on waterbath.

Using a suction pump to remove the last trace of water. Dry residue dissolved in absolute alcohol. Method used in this present investigation is that of Barnet and his co-workers (1946).

For normal results the extracts are dissolved in 4 cc of absolute alcohol and the unknown extract is dissolved in H.C.C. of absolute alcohol 0.2 cc of the 4 cc extract is taken and 0.2DNB and 0.2c alcoholic KOH added. Solution is incubated at 25 ^{o} C for one hour and then made up to a final volume of 10 cc with absolute alcohol.

The Readings are taken on Unicam at 430 m/u for violet, 520 m/u for green. Correcting formula for the interference of xanthocromic materials is observed green - 0 6 violet.

Corrected extinction (green) is then read off from the standard curve (Fig. No. 17 - page 117). This gives the number of green m/u 17 - ketosteroids in 02 of extract. This figure is then multiplied by 20 that corresponds to 4 cc. of extract.

This 4 cc. of extract is from 100 cc. of urine. Hence knowing the

the volume of urine for 24 hours the number in mg of 17 ketosteroids per diem is found out. Normal androgen excrition in male is 14 mg and in female 7 mg as found out in Dr. Stewart's laboratory in Edinburgh.

Estimation of androgen in 24 hours urine has been carried out in 20 cases of various skin diseases (Table No. XXI - page 115). Estimation of androgen has been done in 6 acne vulgaris patients before and 3 months after starting vitamin A therapy (Table NO. XXXII - page 116).

Blood vitamin A estimation and urinary androgen estimation in a case of acne vulgaris during follow-up into vitamin A (Table No. XXIII page 114). Blood vitamin A estimation and urinary androgen estimation in a resistant case of acne vulgaris during follow-up into vitamin A therapy (Table No. XXXIV - page 114) and is shown by curves (Fig. No. 15 page 118).

Table No. XXXIII.

Blood vit. A and urinary androgen during follow-up every month. (Ordinary acne vulgaris).

Estimation of	Before Treat.	End of 1st Month	End of 2nd month	End of 3rd month	End of 4th month.
Blood vit.A	160•4	162•6	190•2	210•0	140•2
Urinary Androgen	22•08	14•00	11•96	6•72	6•64

Table No. XXXIV.

Blood vit. A and urinary androgen during follow-up every month. (Resistant acne vulgaris).

Estimation of	Before Treat.	End of 1st Month	End of 2nd month	End of 3rd month	End of 4th month	End of 5th month	End of 6th month
Blood vit.A	176•0	180•2	174•4	178•8	182•2	180•4	200•2
Androgen estimation	27•00	28•12	28•10	24•22	28•21	20•20	8•00

Table No. XXXI.

ESTIMATION OF ANDROGEN EXCRETION IN SOME SKIN DISEASES.

No.	Name	Sex	Age	Occupation	Disease	Amount of urine in 24 hours in cc.	Violet Inst. Read at 430 m/u	Green Inst. Read at 520 m/u	17-Ketosteroid in mg in 24 hours.
1.	M.W.	F.	25	Housewife	Diss. Lup. Ery.	95·0	0·122	0·520	2·565
2.	C.	F.	30	Housewife	Do	470	0·084	0·080	1·316
3.	F.B.	F.	35	Housewife	Do	1, 250	0·092	0·085	3·500
4.	E.P.	F.	30	Housewife	Ch. Lup. Ery.	1,200	0·115	0·132	3·600
5.	M.R.	F.	57	Housewife	Do	1,100	0·096	0·093	3·75
6.	I.L.	F.	28	Clerkess	Do	9,20	0·110	0·140	6·44
7.	J.G.	F.	37	Weaver	Do	600	0·145	0·190	6·24
8.	J.G.	F.	49	Housewife	Neuroderm.	550	0·090	0·104	2·64
9.	E.S.	F.	41	Housewife	Do	2,400	0·550	0·064	6·72
10.	H.L.	F.	24	Typist	Acne Vulgaris	1,300	0·105	0·162	11·96
11.	I.McD.	F.	15	Com. Artist	Do	1,100	0·110	0·160	9·90
12.	J.F.	F.	19	Univ. Student	Do	900	0·160	0·212	9·90
13.	E.W.	F.	16	Clerkess	Do	1, 080	0·200	0·372	12·96
14.	N.McD.	M.	16	School Student	Do	2000	0·107	0·138	14·00
15.	S.L.	F.	35	Housewife	Do	1130	0·095	0·158	12·00
16.	J.S.	F.	35	Domestic Worker	Psoriaris	1030	0·153	0·183	4,223
17.	C.W.	F.	30	Clerkess	Do	600	0·190	0·270	4·320
18.	E.H.	M.	27	Clerk	Do	800	0·290	0·475	22·08
19.	B.McM.	F.	44	Housewife	Pity.Rub.Pil,	1100	0·085	0·148	11·00
20.	W.H.	M.	32	Factory Worker	Acne Vulgaris	1060	0·200	0·372	12·84

Table No. XXXII.

ESTIMATION OF ANDROGEN EXCRETION IN CASES OF ACNE VULGARIS BEFORE STARTING AND AFTER COMPLETING VITAMIN-A THERAPY.

No.	Name	Sex	Age	Occupation	Before starting Treatment	After completing Treatment.
1.	E.T.	F.	21	Civil Servant	16.45	2.60
2.	A.McG.	F.	15	School Girl	14.00	2.16
3.	P.G.	F.	25	Housewife	17.42	3.14
4.	A.W.	F.	20	Typist	19.41	3.01
5.	R.R.	M.	19	Service	19.54	2.71
6.	W.T.	M.	22	Service	22.41	3.48

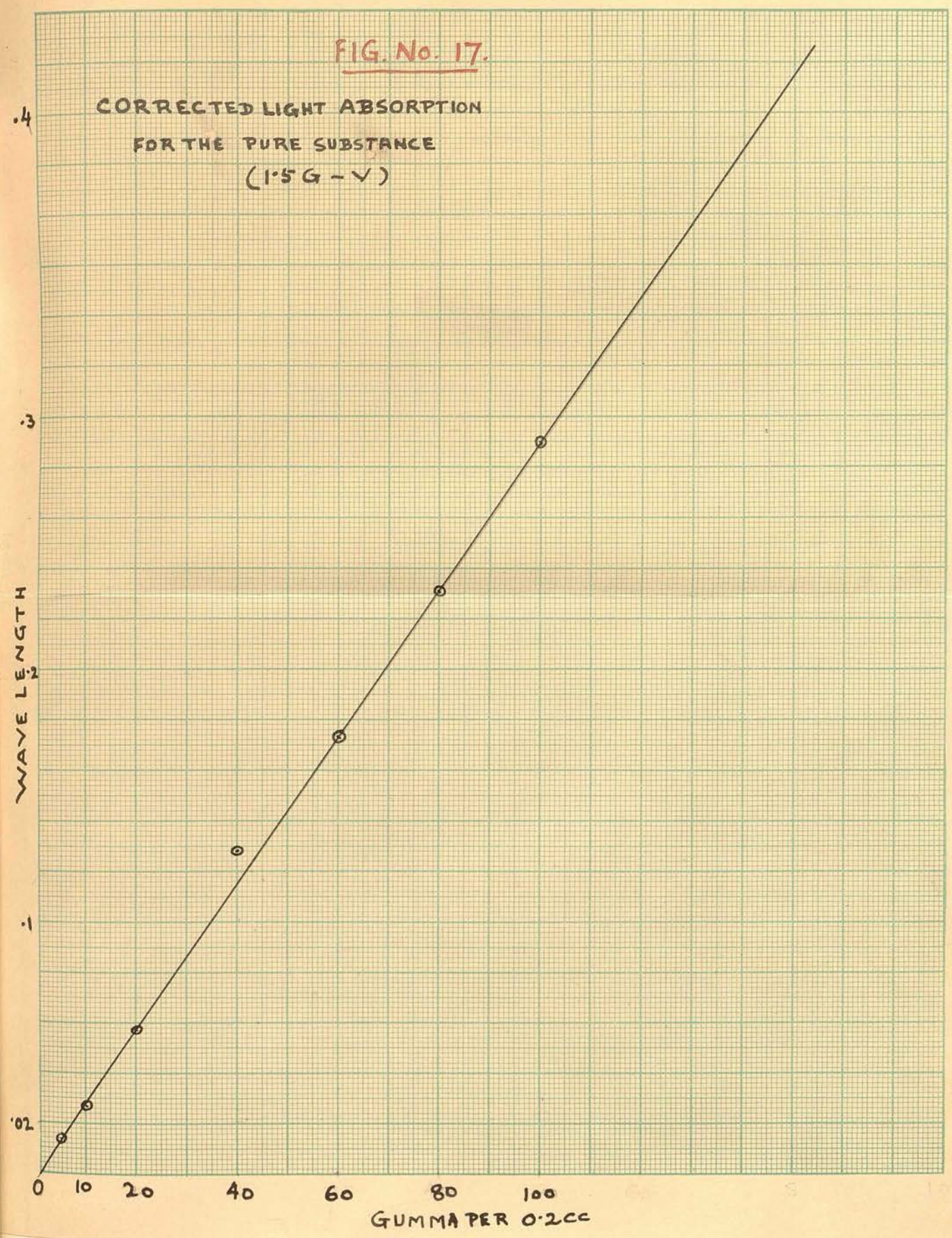


Fig. No. 17. Standard curve for 17- Ketosteroid.

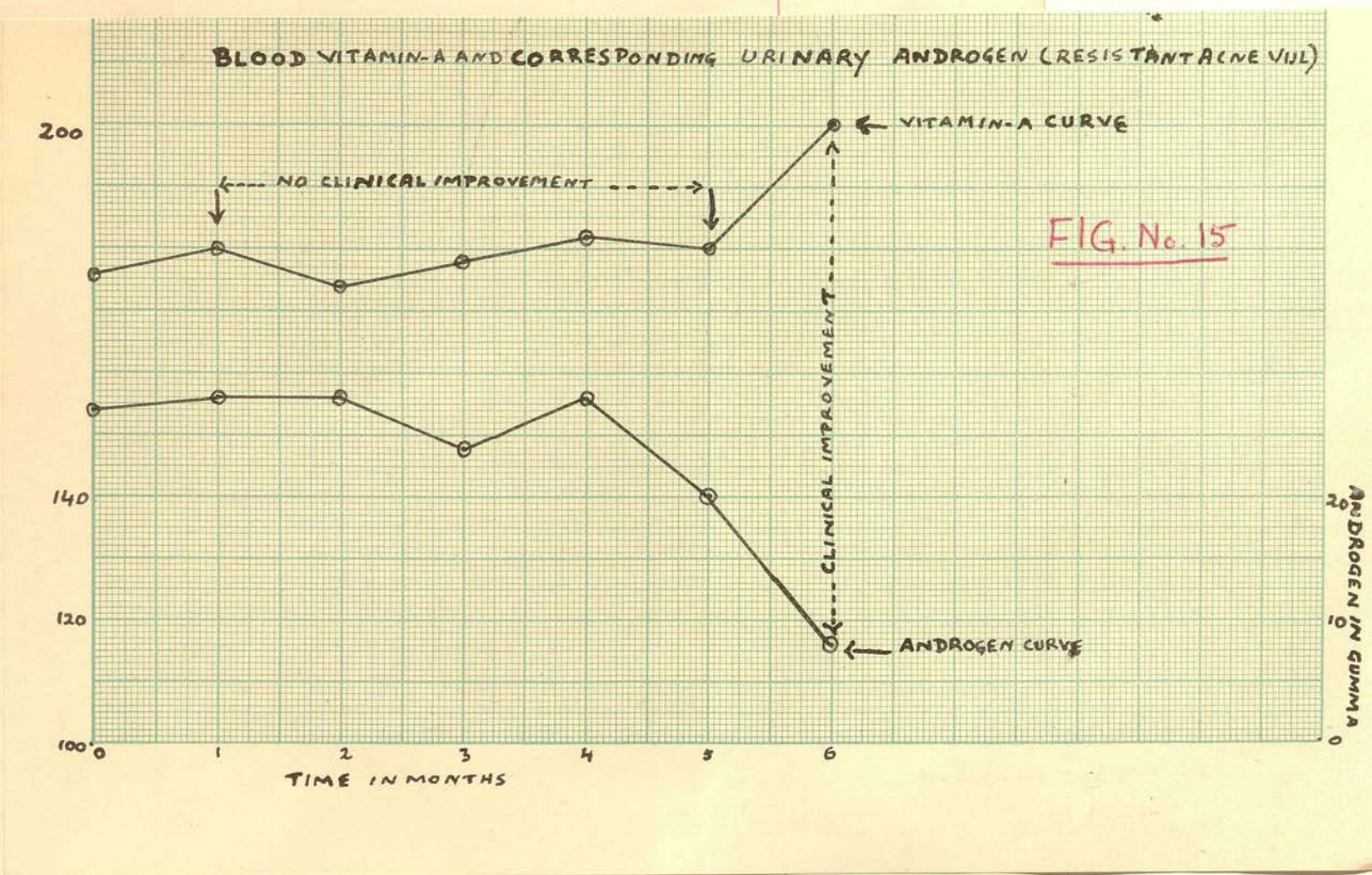


Fig No. 15. Blood aitamin A and urinary androgen estimations in a Resistant case of Acne vulgaris during follow-up with vitamin A therapy.

OBSERVATION

VITAMIN A ESTIMATION: This has been done in the blood by using Carr-Price method and G.D.H. method with the help of a very sensitive instrument.

METHODS COMPARED: The Carr-Price method has various drawbacks such as (1) the blue colour which develops by the interaction of vitamin A with antimony trichloride stays only for 5 seconds making the correct reading of the intensity of the colour difficult, (2) the reagent absorbs moisture and becomes turbid, (3) even with the sensitive Unicam instrument the Carr-Price method gives a low vitamin A value with or without saponification and (4) saponification of serum is necessary for 60 minutes.

SAPONIFICATION: Saponification of the serum for different lengths of time gives different vitamin A values with Carr-Price method. With the Carr-Price method of estimation of vitamin A the unsaponified serum gives a very low value for vitamin A than in serum by saponifying for 20 minutes and for 60 minutes.

With G.D.H. method there is practically no difference in vitamin A values of the unsaponified serum when compared with serum saponified for 60 minutes with Carr-Price method.

The G.D.H. value of vitamin A of unsaponified serum is similar to the Carr-Price value of vitamin A in serum saponified for 60 minutes.

Hence for the assessment of vitamin A nutrition in the present investigation unsaponified serum with

modified G.D.H. method has been used.

Vitamin A nutrition has been estimated in 114 normal human subjects of adult age (Tables Nos. XIII - page 78 and XIV - page 82).

Blood vitamin A and carotene have been estimated in 56 normal human males (Table No. XIII - page 78).

Average Vitamin A = 200 Int. unit per 100 cc. of blood.

" Carotene = 60 " " " " "

Statistically the standard deviation being - 17.9 for carotene and - 48.4 for vitamin A.

Blood vitamin A and carotene have been estimated in 58 normal human females (Table No. XIV - page 82).

Average Vitamin A = 174 Int. unit per 100 cc. of blood.

" Carotene = 71 " " " " "

Statistically the standard deviation being - 26.1 for carotene and - 48.7 for vitamin A.

For 114 mixed normal human subjects:-

Average Vitamin A being 187 I.U. per 100 cc. of blood.

" Carotene " 68 " " " " " "

The range of vitamin A being 72 I.U. to 301 I.U.

" carotene " 21 " " 153 "

Vitamin A clearance test has been observed by the administration of 100,000 Int. Unit vitamin A orally and in the same case by administration of the same dose of vitamin A parenterally after one week (Fig. No. 9 - page 106). Oral method shows better value and thus reflects better utilization of vitamin A.

It has been possible to investigate 170 patients

of skin diseases supposed to be due to some disturbance of vitamin A nutrition (Table No. XXXV - page 121).

Table No.XXXV

The cases of skin diseases showing average vitamin A and carotene:

No.	Name of Skin Disease	No. of Cases	Average Vitamin A	Average Carotene
1	Ichthyosis	9	131.0 I.U.	73.3 I.U.
2	Pityriasis Rubra Pilaris	1	84.5 I.U.	25.0 I.U.
3	Nummular Eczema	15	115.6 I.U.	59.0. I.U.
4	Acne Vulgaris	75	175.0 I.U.	75.0 I.U.
5	Besnier's Prurigo	16	195.0 I.U.	56.0 I.U.
6	Neurodermatitis	7	190.0 I.U.	49.0 I.U.
7	Alopecia Arcata and) Pseura Palada de Broq)	7	175.0 I.U.	67.0 I.U.
8	Lupns Erythermatosis	6	210.0 I.U.	38.7 I.U.
9	Keratoderma Palmaris et Plantaris	2	212.0 I.U.	65.0 I.U.
10	Lichen Planus	15	252.0 I.U.	81.2 I.U.
11	Psoriasis	17	223.0 I.U.	57.5 I.U.

These 170 patients of different types of skin diseases may be divided into 3 different groups such as:- (1) Showing low vitamin A nutrition, such as are the cases of ichthyosis, pityriasis rubra pilaris and nummular eczema, (2) showing almost normal vitamin A nutrition such as are the cases of acne vulgaris, Besnier's prurigo, neurodermatitis, alopecia ariata and pseuda pelade de Brocq and (3) showing higher

vitamin A nutrition such as are the cases of psoriasis, lichen planus, keratoderma palmaris et planlaris and lupns vulgaris.

LOW VITAMIN A NUTRITION

ICHTHYOSIS: 9 cases of ichthyosis exhibiting mild, moderate and only one of severe grades have been investigated. All the cases show low blood vitamin A, and normal carotene content.

Vitamin A therefore orally in dose of 100,000 I.U. daily for a period of 3 months cured 6 and improved all. Only 2 cases relapsed. Skin felt moist and smooth with amelioration of symptoms.

NUMMULAR ECZEMA: 15 cases have been investigated. The average blood vitamin A value is lower than the normal whereas the carotene value is slightly lower than the normal.

All the cases showed dry skin and the nummular eczema of hand and legs were on an average of 2 years old.

All the cases responded on an average period of 3 months with only oral therapy of vitamin A 100,000 I.U. per day. 2 cases took 7 months to clear and only one relapsed after about one year.

PITYRIASIS RUBRA PILARIS: It is a very rare disease in Great Britain though Percival (1950) believes that subclinical types are frequently met with.

The only one case has been investigated in the

present series. Since it is a rare and very interesting case a short history is given below.

Mrs B. MacM., 44 years old, housewife from East Lothian in Scotland, was admitted in the Skin Department of the Edinburgh Royal Infirmary on the 20th December 1949 under Professor Percival.

Family history - Husband living and healthy. Has a family of one child - son, 24 years old, and is healthy. None in the family either on her mother's side or on the father's side had any history of skin disease, hay fever, asthma, or any illness.

Personal history - Menarche at 13 years and her periods have never troubled her and has not stopped yet.

History of present illness - In October 1949 the disease started as a 'hak' (fissure) on both knees. Then the heels cracked. Within a few days right side of the face got swollen up and hairs started falling from her head. Within a month her face, body and legs got swollen up when she was sent to the hospital by her doctor.

Examination revealed a typical acute case of pityriasis rubra pilaris. Face was puffy and waxy-looking. Palms and soles were very much hyperkeratotic. The whole body including trunk and upper and lower limbs showed areas of healthy skin with extensive areas of slightly crusted areas. Nails were greyish and rough.

Slight oozing could be seen on the front of the

elbows.

Cardiovascular system - pulse 70, no abnormality.

Gastrointestinal system - bowels all right, appetite good.

Urinary system - no difficulty or frequency of micturition.

On 2.1.50 examination of urine normal.

C.N.S. - no abnormality seen.

INVESTIGATION

5 cc. of blood was taken from cubital vein in January 1950 for vitamin A estimation and 24 hours urine collected for androgen estimation. Blood vitamin A was low; with a view to quicken the result vitamin A by intramuscular injection in dose of 100,000 in daily started and blood vitamin A was estimated after 2 weeks but there was no appreciable change in blood vitamin A level (Fig. No. 10).

Vitamin A in the same dose started orally giving 50,000 in morning and evening at 12 hours interval and blood vitamin A was estimated after 2 weeks, that is, one month after starting vitamin A therapy and the estimation was repeated at monthly intervals which showed steady rise of vitamin A value of blood (Fig. No. 10).

The skin condition of the patient was greatly improved and the patient was discharged from the hospital in the second month of vitamin A treatment, that is, in February 1950.

Patient came every month for examination and

every time her blood vitamin A was estimated which showed a steady rise up to the fourth month when the amount of vitamin A was reduced to half daily dose. At the end of the fifth month of treatment the patient was free of any skin lesion except slight hyperkeratosis of palms and soles and the blood level of vitamin A has come down slightly as shown in the vitamin A curve (Fig. No. 10 -page 126).

Androgen excretion was done only twice.

At the end of the first month and end of the fourth month of vitamin A treatment, the values being 22 and at the end of first month which came down to 6 and at the end of fourth month of treatment.

Photos taken before discharge of the patient from the hospital (Figs. Nos. 18 and 18 - page 127) during the second month of treatment and again at the end of fifth month of treatment show definite improvement of skin lesions both on the trunk and palm and hyperkeratosis (Figs. Nos. 19A and 19B - page 127).

Cases of pityriasis rubra pilaris have relationship with vitamin A has been shown by a large number of dermatologists both in Great Britain and America (Brunsting and Sheard, 1941; Peck and Chargin, 1941; Leitner, 1946). Moore (1941) found low blood vitamin A level. Low plasma vitamin A has been observed in pityriasis rubra pilaris by Leitner and Moore (1946). Mitchell-Heggs and Feiwel (1947) reported a case of pityriasis rubra pilaris in which

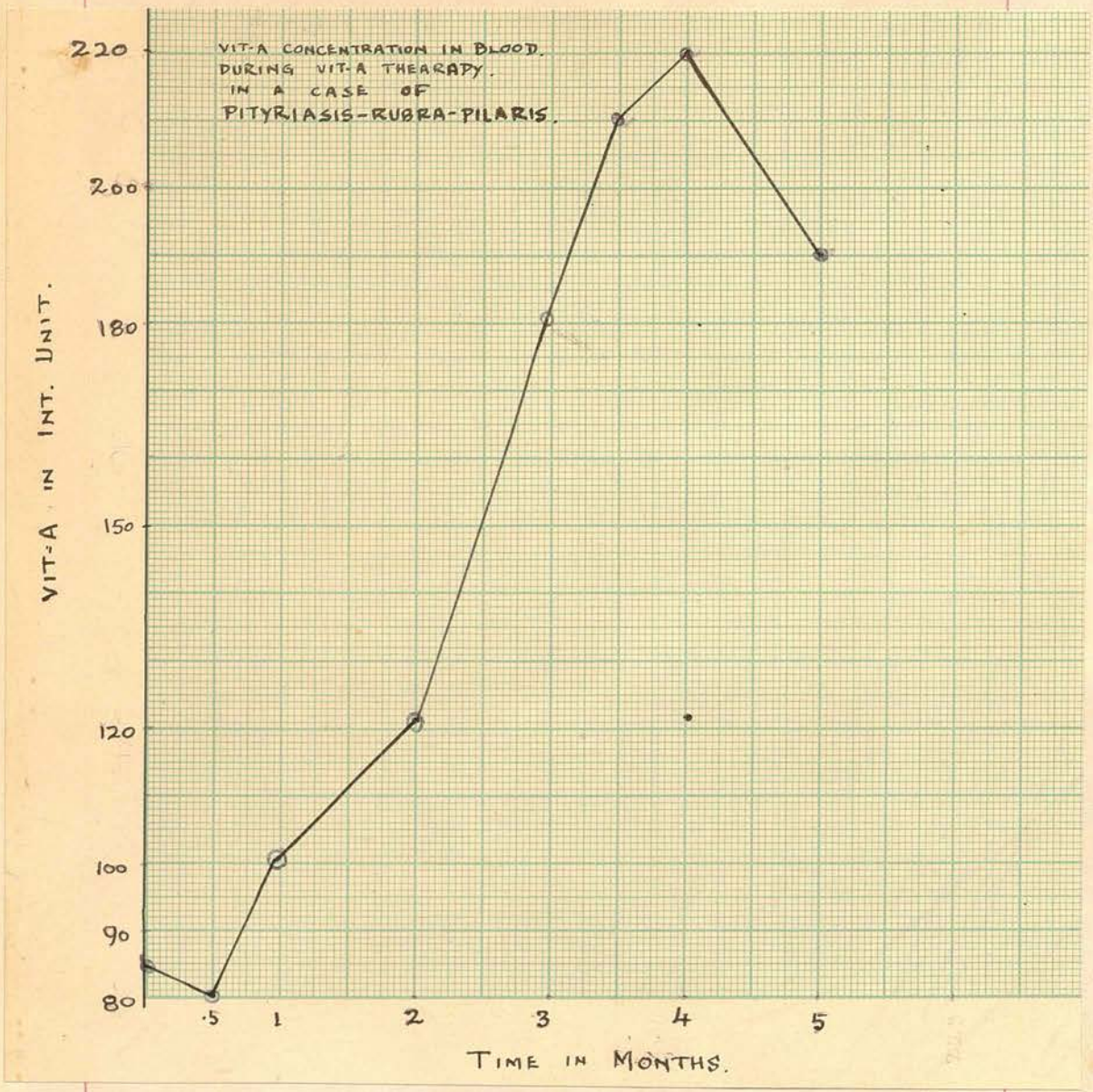


Fig. No. 10. Curve indicating rise of blood vitamin A with intramas cular vitamin A for 2 weeks and then after same dose orally up to 4 months with steady clinical improvement and dose was reduced at the end of the fourth month vitamin concentrate in blood at the end of the fifth month has come down with maintained clinical improvement.

Fig. No. 18A Mrs. B. McM.
Before treatment of Pityriaris rubra pilaris.

Fig. No. 18B. Mrs. B. McM.
After treatment.

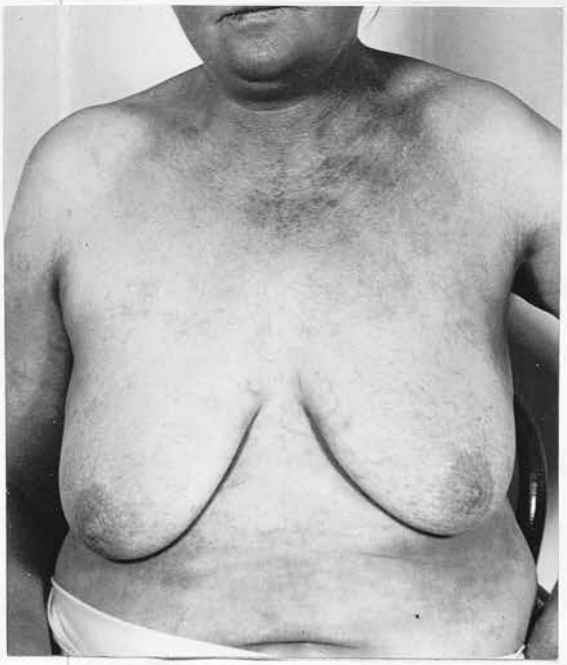


Fig. No. 19A. Mrs. B.McM.
Before treatment of Pit. rubra pil.

Fig. No. 19B. Mrs. B. McM.
After treatment.

vitamin A was found normal.

Knowles (1949) has observed improvement in pityriasis rubra pilaris with vitamin A therapy. Cornbleet and his associates (1947) have treated a case with an enormously high dose of vitamin A for a long period.

In the case under review in the prime investigation low blood vitamin A has been observed. Improvement in skin condition with rise of blood vitamin A level has been found with high dose of vitamin A therapy. Moore (1941) and again Leitner and Moore (1946) have found low blood vitamin A in pityriasis rubra pilaris. In the case of Mitchell-Heggs and Feiwel (1947) normal blood vitamin A has been found.

NORMAL VITAMIN A NUTRITION

ACNE VULGARIS: 75 cases of acne vulgaris have been investigated. In each case blood vitamin A and carotene have been estimated and patient put on 100,000 I.U. of vitamin A orally per day for a period of 3 months.

In 75 cases of acne vulgaris values for blood vitamin A being 175.0 Int. Unit per 100 cc. blood, and carotene being 59.0 Int. Unit per 100 cc. blood.

Statistically mean deviation being - 52.5 for vitamin A and 22.1 for carotene.

Vitamin A values in acne vulgaris cases compared with vitamin A values of normal males and females (Table No.XXXV - page 128).

Table No.XXXV

Table shows comparison of values with normal values.

		Carotene	Mean Vita.A	Mean Carotene
Acne	_ 52.5	_ 22.1	175.1	59.4
Normal Male	_ 84.4	_ 17.9	200.3	65.7
Normal Female	_ 48.7	_ 26.1	174.7	71.6

The blood vitamin A values of acne patients when compared with the values of normal males and females do not show much significance.

Vitamin A clearance when compared with a normal subject shows a much lower peak and a late return to normal (Fig. No. 11 - page 107). The clearance test in six cases of acne vulgaris has been compared with six normal subjects (Fig. No. 12) and a much lower peak compared to the normal peaks and a delayed return to the normal values in blood has been found in cases of acne vulgaris (Fig. No. 12 - page 110).

Urinary androgen in 24 hours urine has been estimated but in 6 cases of acne vulgaris and the values are not very high (Table No. XXXI - page 118).

With vitamin A therapy orally in dose of 100,000 I.U. per day for a period of 3 months 60 cases got well, that is, 80 p.c. patients were cured, and 15 patients improved tremendously, that is, 20 p.c. cases improved out of 75 cases (Fig. No. 13 - page 130).

In a case of acne blood vitamin A and urinary androgen were estimated before starting vitamin A treatment and during the follow-up at the end of

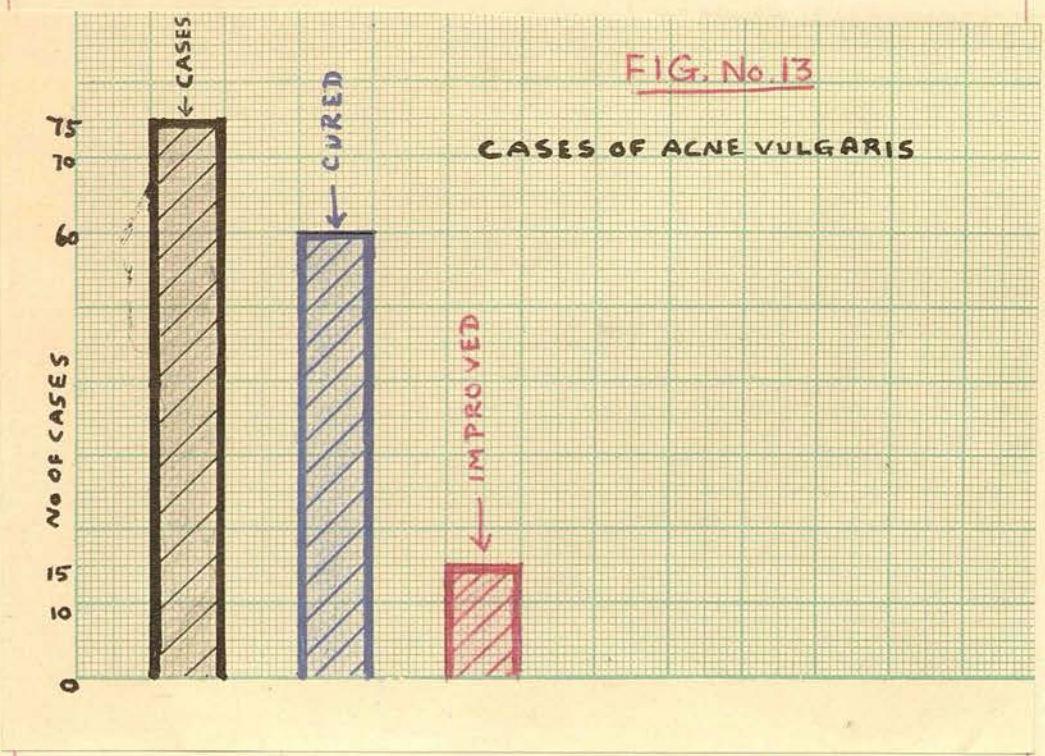


Fig. No. 13. Indicating by light and by black colour the number of cases investigated, by blue colour the number of cases cured and by red colour.

every month blood and urine were examined for vitamin A and androgen respectively for 4 months. The rise in blood vitamin A and gradual fall in urinary adnrogen with vitamin A therapy has been observed (Fig. No. 14 - page 132).

In a resistant case of acne vulgaris blood vitamin A and urinary adnrogen estimations carried during the follow-up while getting vitamin A therapy orally shows higher value of blood vitamin A after a much longer period of time than in ordinary acne vulgaris cases with a consequent fall in the urinary androgen value after a prolonged vitamin A therapy. Improvement observed 5 months after the vitamin A therapy started with high vitamin A value and lower urinary androgen value (Fig. No. 15 - page 118).

The improvement in the clearance test in acne vulgaris after completion of the vitamin A therapy has been observed (Fig. No. 16 - page 111).

Of the 75 cases of acne vulgaris treated with only vitamin A therapy alone 36 are females and 39 are males. Amongst the resistant cases there are 5 females. All had history of either irregularity of menstruation or dysmenorrhoea. Male resistant cases are 11 in number. Each of these 11 cases exhibited thick, slightly myxaedematous skin which returned to the normal texture of the skin with the vitamin A therapy.

With the vitamin A therapy the changes in the skin have been observed earlier than the cure of acne

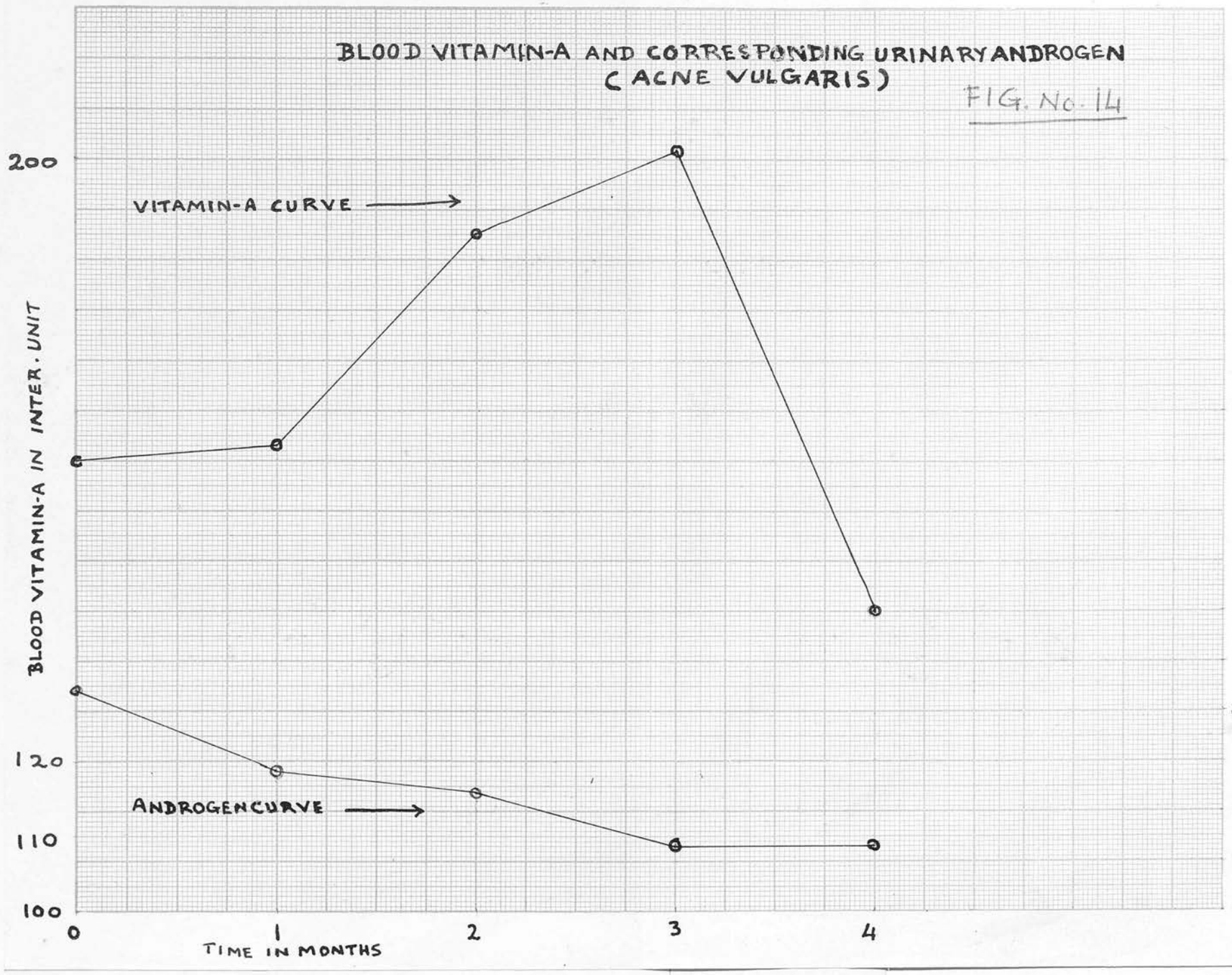


Fig. No. 14 Blood vitamen A and urinary androgen estimations in a follow-up Case of Acne Vulgaris with vitamin A therapy.

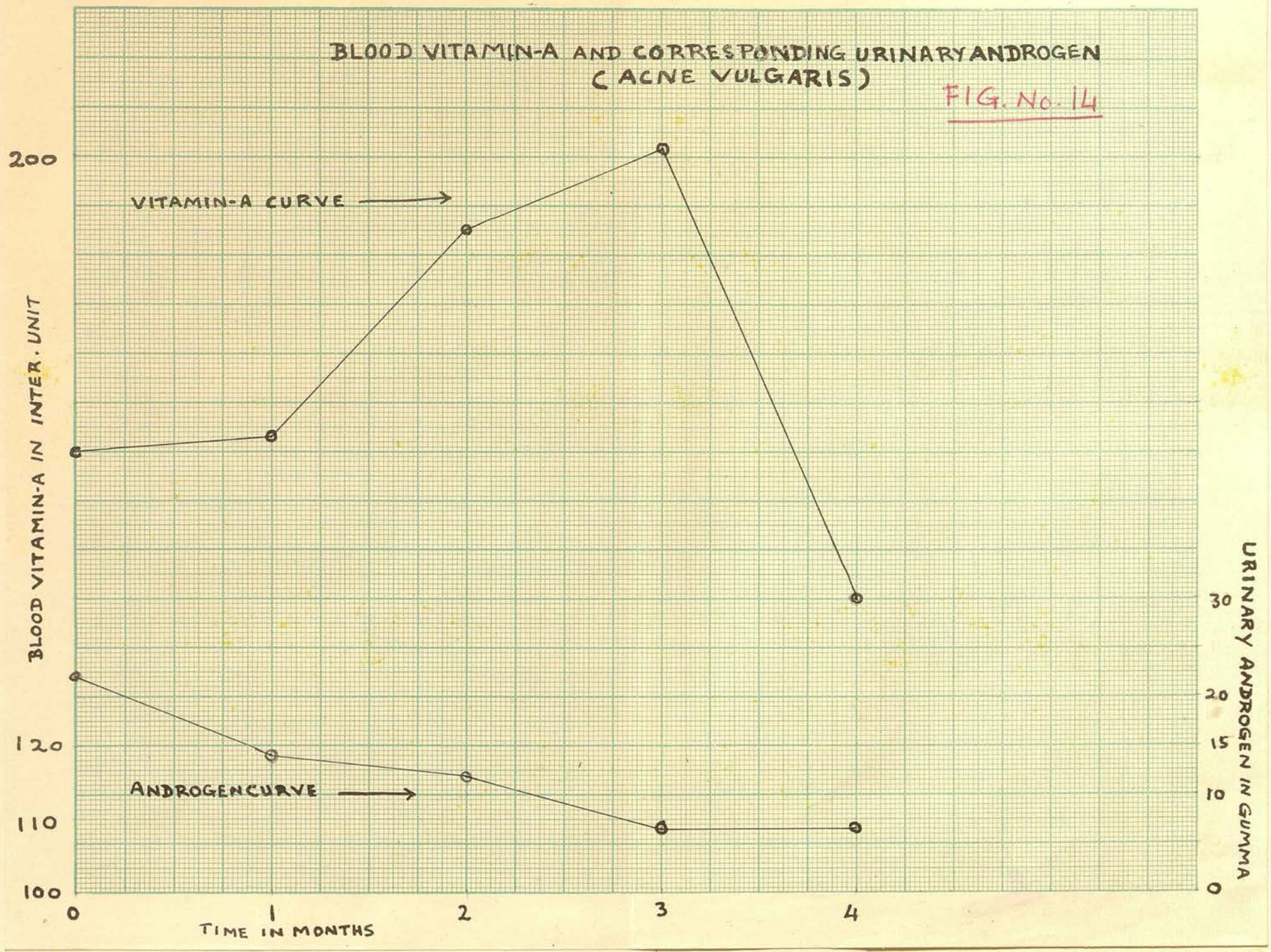


Fig. No. 14 Blood vitamen A and urinary androgen estimations in a follow-up Case of Acne Vulgaris with vitamin A therapy.

vulgaris. Oiliness disappeared on an average time of one month only but the nail changes when present improved after 2 months therapy. Acne vulgaris got well on an average period of 3 months from the starting of vitamin A therapy orally in dose of 100,000 I.U. daily.

In the present series of cases cures have been observed in 80 per cent cases and improvement in 20 per cent cases with only vitamin A therapy in 3 months (Fig. No. 13 - page 130).

The 15 resistant cases of acne vulgaris also improved in 3 months but the vitamin A therapy had to be continued on an average of 4 months for cure in these resistant cases (Table No. XXXVIII - page 159).

Most of the cases improved within 2 months after starting the vitamin A orally but 40 cases took 3 months, 20 for $3\frac{1}{2}$ months, whereas only 10 got well in 2 months and 5 after 4 months (Table No. XXXIX - page 160).

Photos of cases of acne vulgaris, taken before starting and after completion of oral vitamin A theraphy, show improvement in the skin condition (Figs. Nos. 20A - page 134 to Fig. No. 60 - page 154).

Table No. XXXV

Cases of acne vulgaris treated with oral administration of 100,000 I.U. of vitamin A.

No.	Name	Sex	Age	Lesions	Months of Vit.A	Remarks
1	H.L.	F	24	Papules on face	$3\frac{1}{2}$	Cleared completely but only few

Fig. No. 20A. Miss H.L.
Before treatment of Acne Vulgaris.

Fig. No. 20B. Miss H.L.
After treatment.

Fig. No. 21A. Miss H.L.
Before treatment of Acne Vulgaris.

Fig. No. 21B. Miss H.L.
After treatment.

Fig. No. 22A. Miss C.G.
Before treatment of Acne Vulgaris.

Fig. No. 22B. Miss C.G.
After treatment.

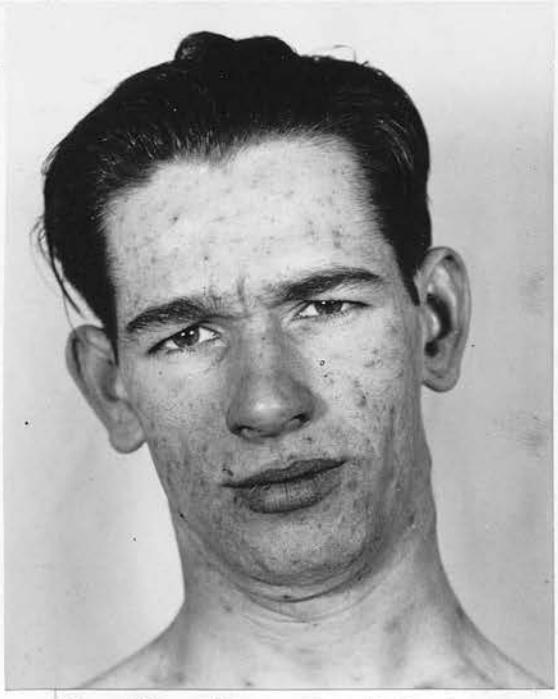


Fig. No. 23A. Mr. W.B.
Before treatment of Acne (cystictype).

Fig. No. 23B. Mr. W.B.
After treatment.

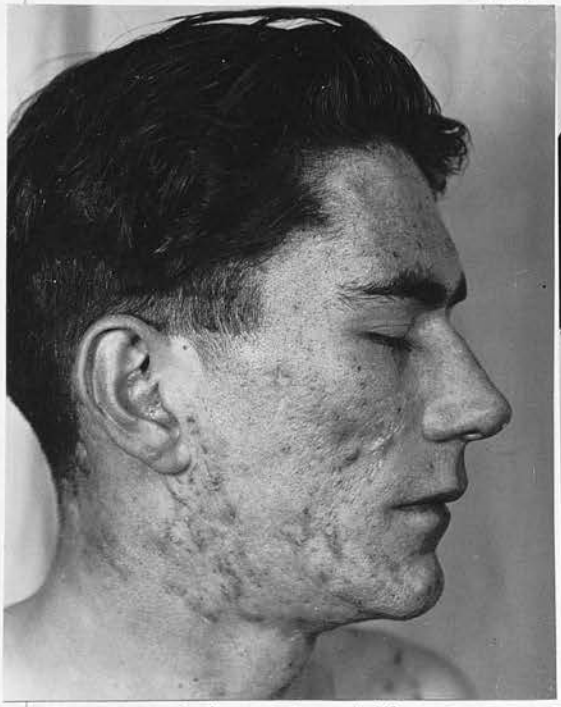


Fig. No. 24A. Mr. A.W.
Before treatment of Acne (cystictype).

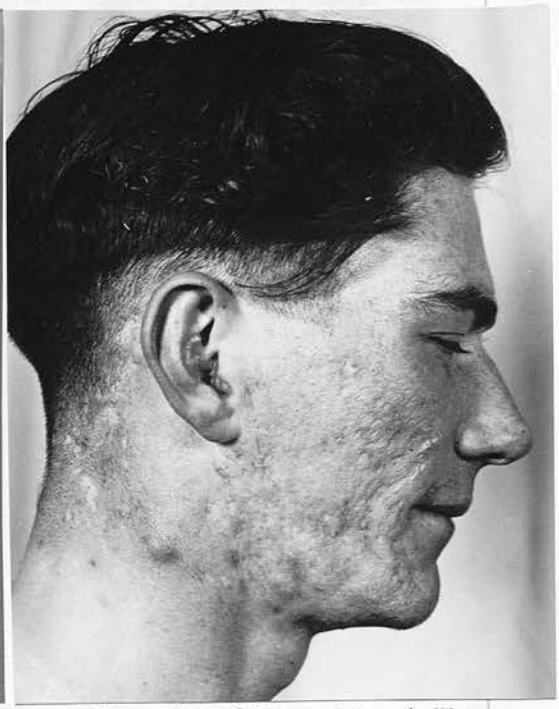


Fig. No. 24B. Mr. A.W.
After treatment.

Fig. No. 25A. Mr. A.W.
Before treatment of Acne (cystictype).

Fig. No. 25B. Mr. A.W.
After treatment.

Fig. No. 26A. Mr. J.T.
Before treatment of Acne Vulgaris.

Fig. No. 26B. Mr. J.T.
After treatment.

Fig. No. 27A. Mr. J.T.
Before treatment of Acne Vulgaris.

Fig. No. 27B. Mr. J.T.
After treatment.

Fig. No. 28A. Mr. W.M.
Before treatment of Acne Vulgaris.

Fig. No. 28B. Mr. W.M.
After treatment.

Fig. No. 29A. Mr. J.M.
Before treatment of Acne Vulgaris.

Fig. No. 29B. Mr. J.M.
After treatment.

Fig. No. 30A. Mrs. S.L.
Before treatment of Acne Vulgaris.

Fig. No. 30B. Mrs. S.L.
After treatment.

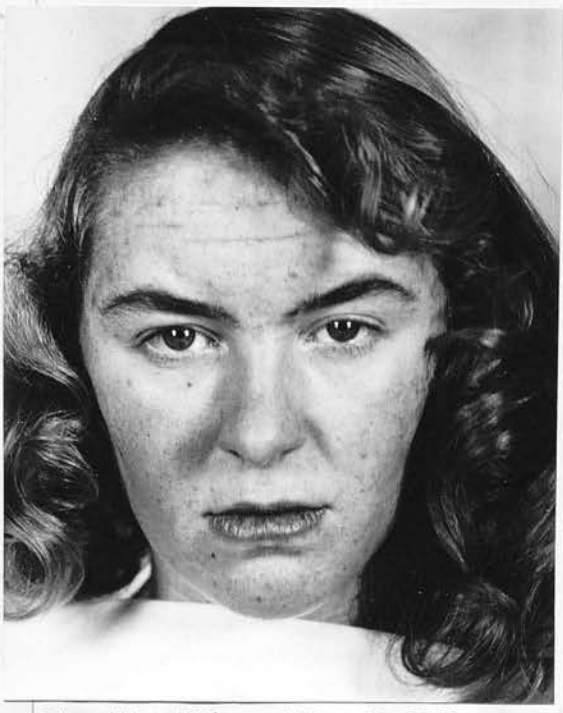


Fig. No. 31A. Miss I. McD.
Before treatment in Acne Vulgaris.

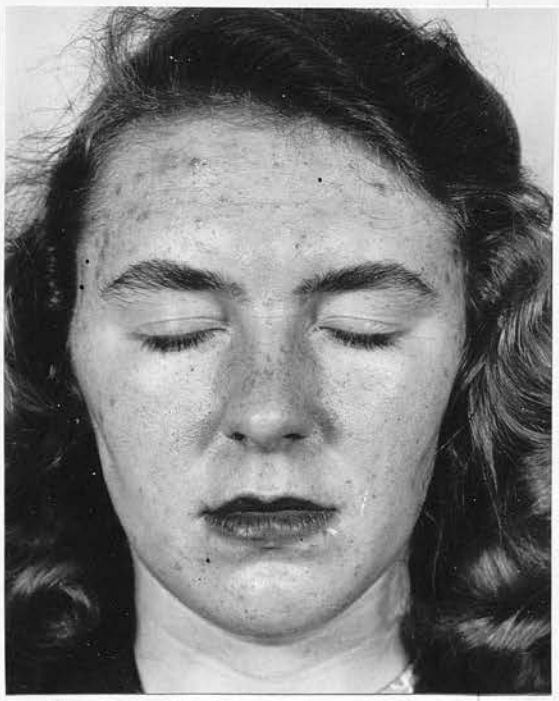


Fig. No. 31A. Miss I. McD.
After treatment.

Fig. No. 32A. Mr. J.M.
Before treatment of Acne Vulgaris.

Fig. No. 32B. Mr. J.M.
After treatment.

Fig. No. 33A. Mr. R.R.
Before treatment of Acne Vulgaris.

Fig. No. 33B. Mr. R.R.
After treatment.

Fig. No. 34A. Miss W.F.
Before treatment of Acne Vulgaris.

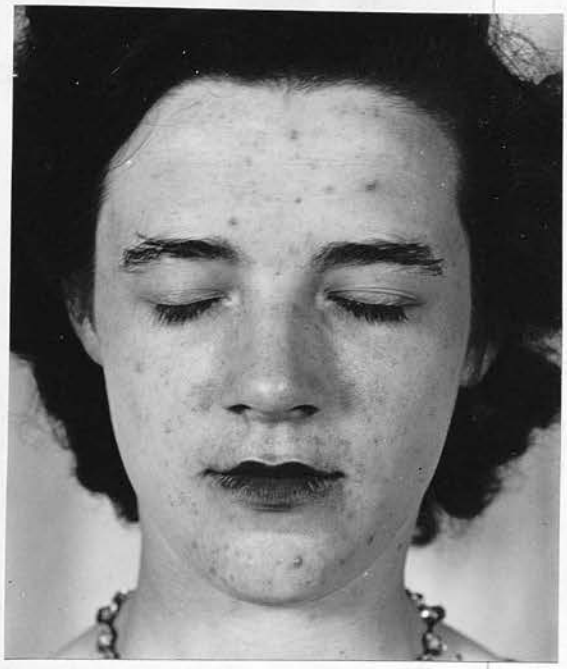


Fig. No. 34B. Miss W.F.
After treatment.

Fig. No. 35A. Miss E.B.
Before treatment of Acne Vulgaris.

Fig. No. 35B. Miss E.B.
After treatment.

Fig. No. 36A. Mr. R.R.
Before treatment of Acne Vulgaris.

Fig. No. 36B. Mr. R.R.
After treatment.

Fig. No. 37A. Mr. J.C.
Before treatment of Acne Vulgaris.

Fig. No. 37B. Mr. J.C.
After treatment.

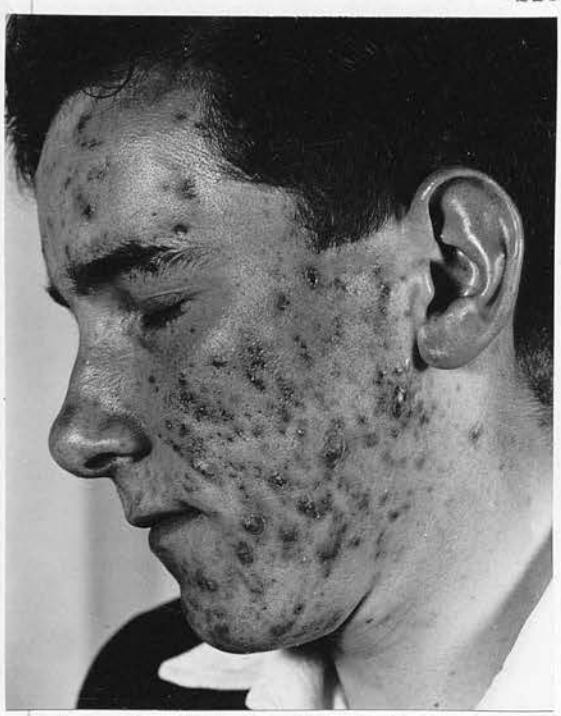


Fig. No. 38A. Mr. G.T.
Before treatment of Acne (cystictype).

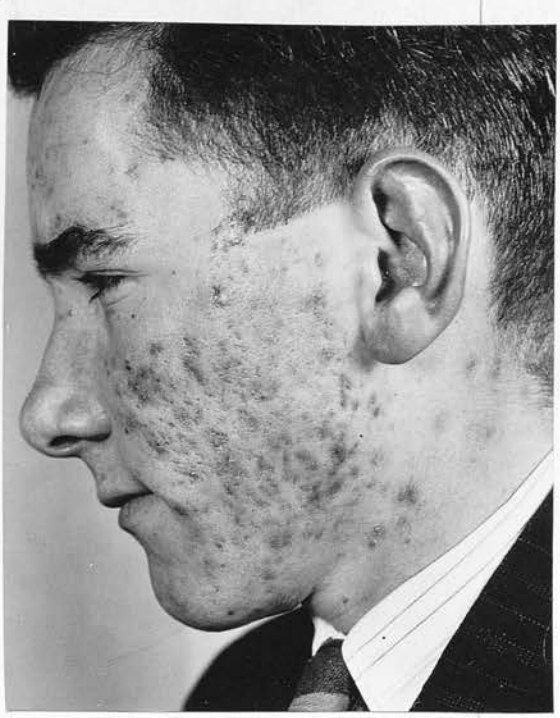


Fig. No. 38B. Mr. G.T.
After treatment.

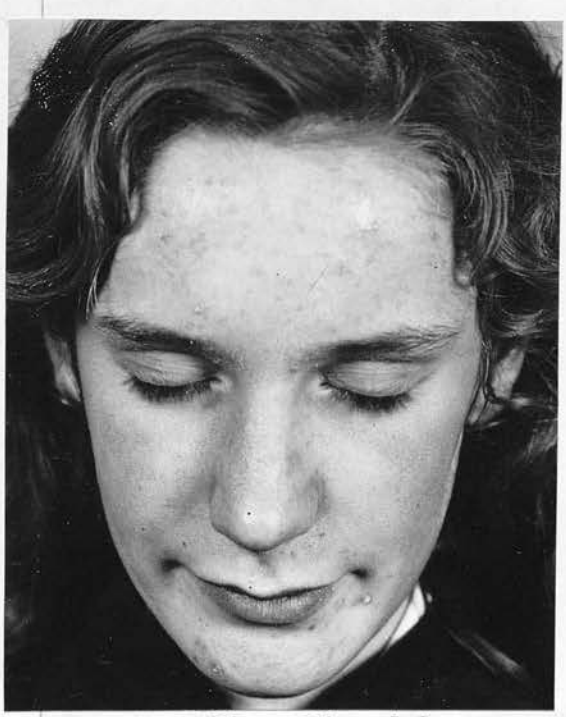


Fig. No. 39A. Miss J.C.
Before treatment of Acne Vulgaris.

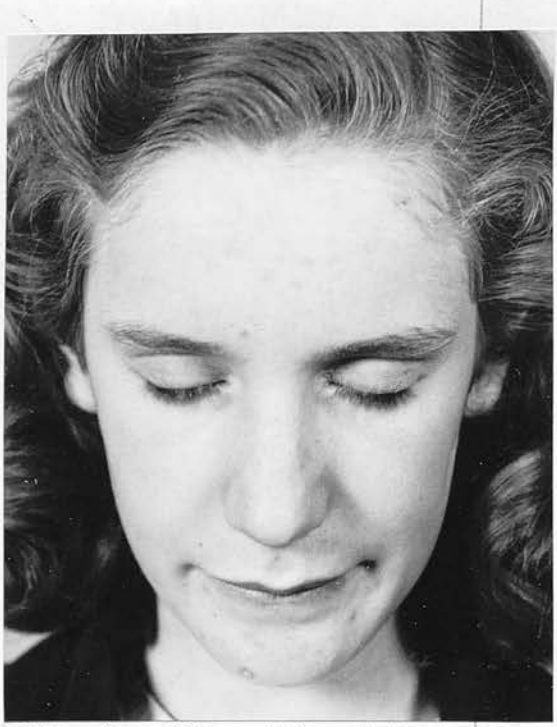


Fig. No. 39B. Miss J.C.
After treatment.

Fig. No. 40A. Miss M.L.
Before treatment of Acne Vulgaris.

Fig. No. 40B. Miss M.L.
After treatment.

Fig. No. 41A. Miss J.M.
Before treatment of Acne Vulgaris.

Fig. No. 41B. Miss J.M.
After treatment.

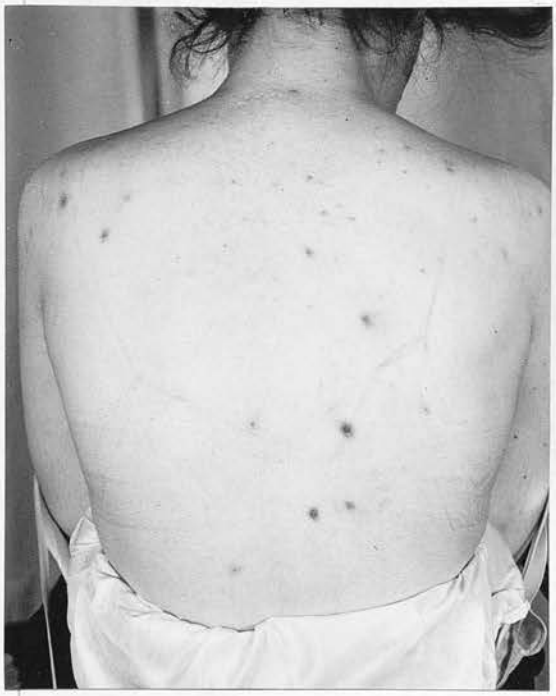


Fig. No. 42A. Miss B.
Before treatment of Acne Vulgaris.

Fig. No. 42B. Miss B.
After treatment.

Fig. No. 43A. Miss E.T.
Before treatment of Acne Vulgaris.

Fig. No. 43B. Miss E.T.
After treatment.

Fig. No. 44A. Miss E.W.
Before treatment of Acne Vulgaris.

Fig. No. 44B. Miss E.W.
After treatment.

Fig. No. 45A. Mr. D.M.
Before treatment of Acne Vulgaris.

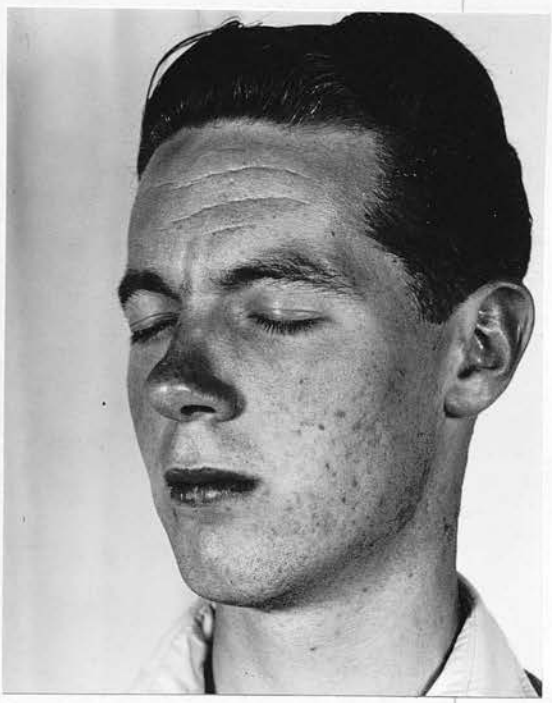


Fig. No. 45B. Mr. D.M.
After treatment.

Fig. No. 46A. Miss M.B.
Before treatment of Acne Vulgaris.

Fig. No. 46B. Miss M.B.
After treatment.

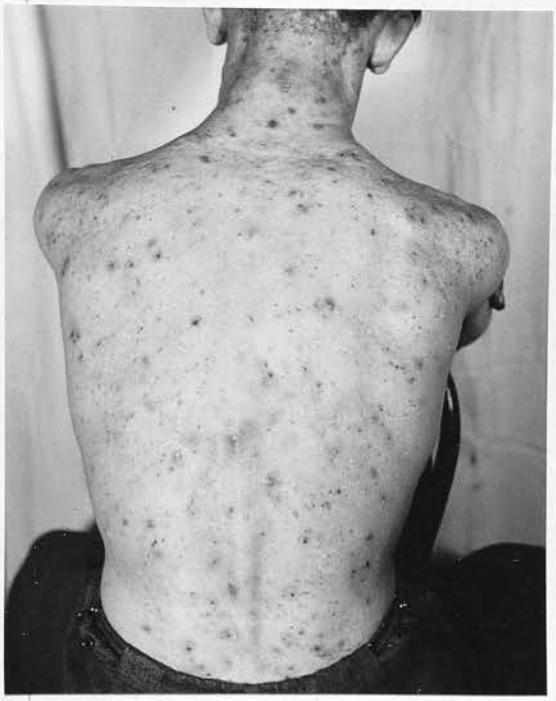


Fig. No. 47A. Mr. J.I.
Before treatment of Acne Vulgaris, with blackheads.

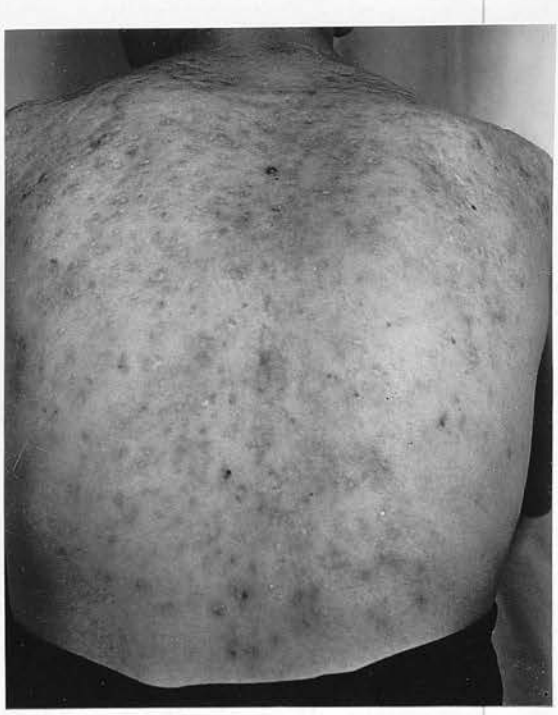


Fig. No. 47B. Mr. J.I.
After treatment.

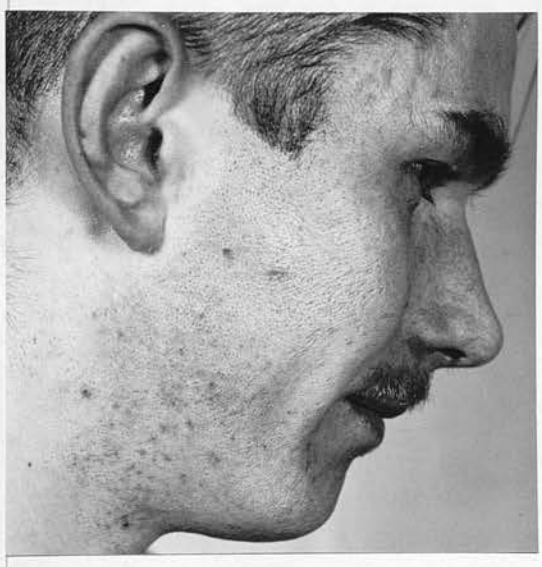


Fig. No. 48A. Mr. G.Q.
Before treatment of Acne Vulgaris.

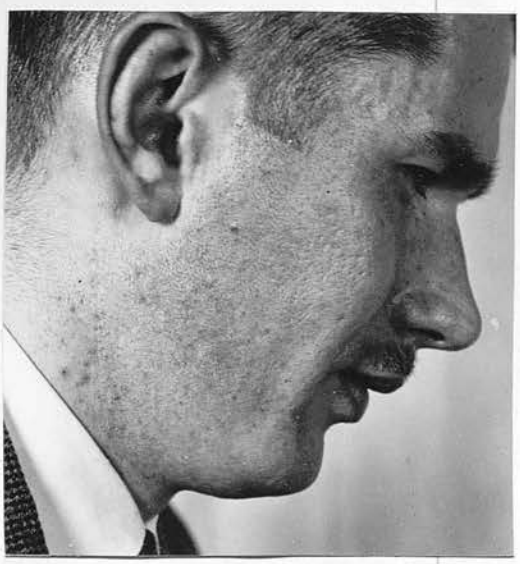


Fig. No. 48B. Mr. G.Q.
After treatment.

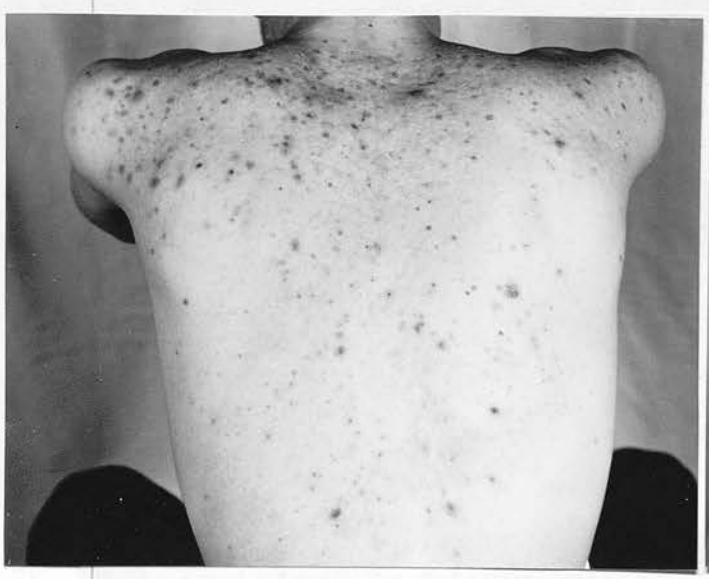


Fig. No. 49A. Mr. G.Q.
Before treatment of Acne Vulgaris.

Fig. No. 49B. Mr. G.Q.
After treatment.

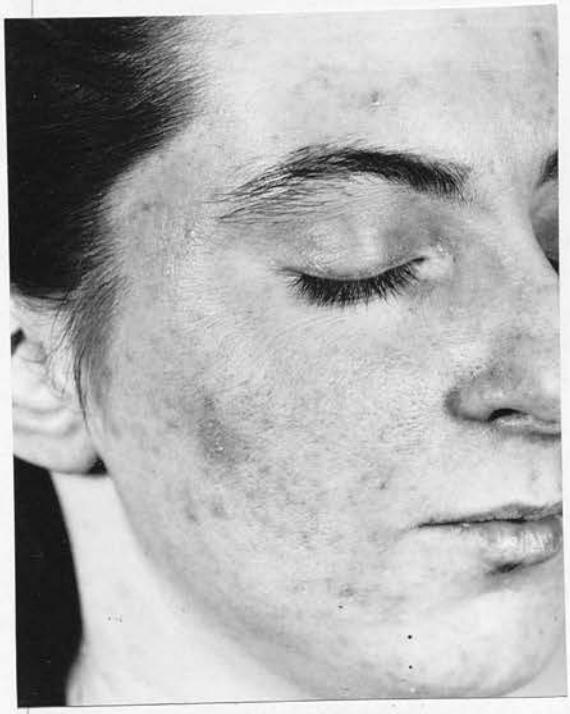


Fig. No. 50A. Miss J.M.
Before treatment of Acne Vulgaris.

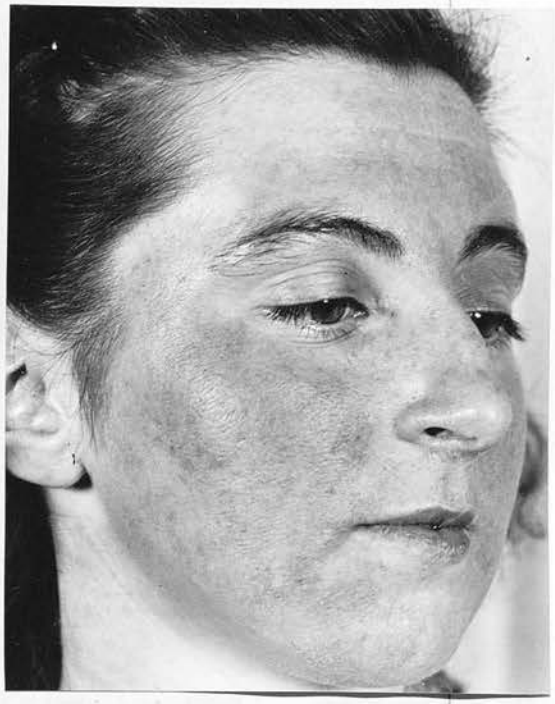


Fig. No. 50B. Miss J.M.
After treatment.

Fig. No. 51A. Miss J.M.
Before treatment of Acne Vulgaris.

Fig. No. 51B. Miss J.M.
After treatment.

Fig. No. 52A. Miss J.B.
Before treatment of Acne Vulgaris.

Fig. No. 52B. Miss J.B.
After treatment.

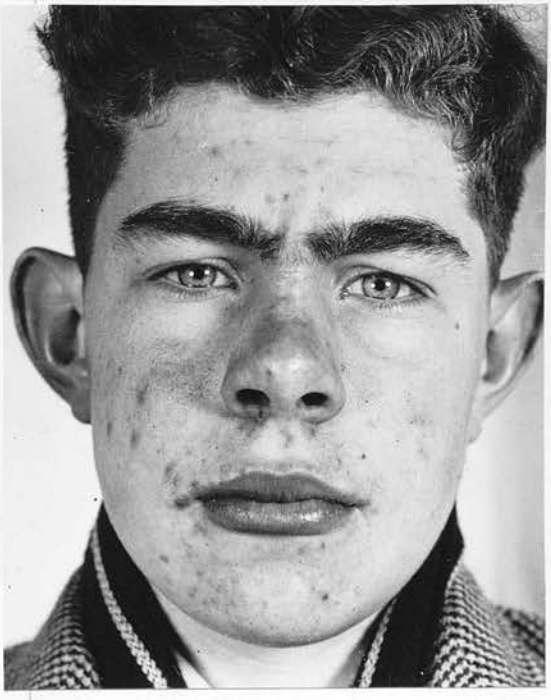


Fig. No. 53A. Mr. N.O.
Before treatment of Acne Vulgaris.

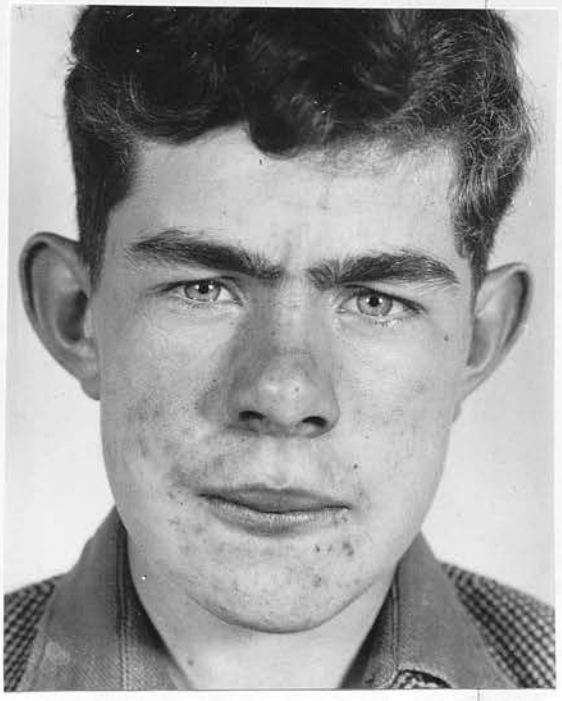


Fig. No. 53B. Mr. N.D.
After treatment.

Fig. No. 54A. Mr. L.W.
Before treatment of Acne Vulgaris.

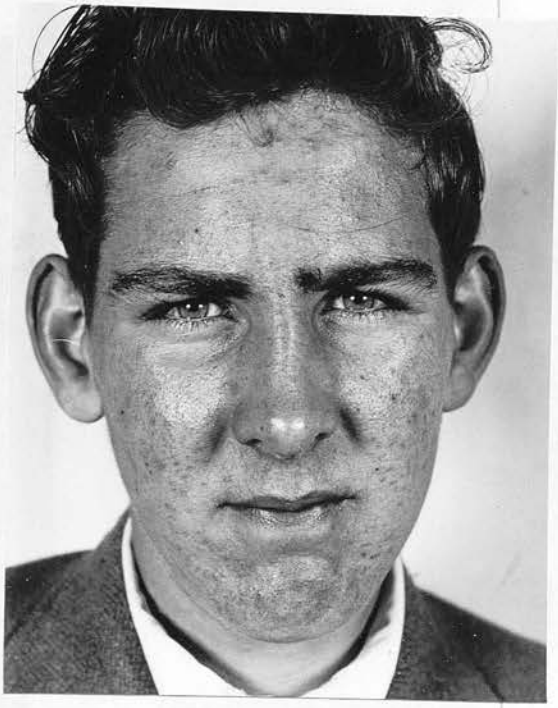


Fig. No. 54B. Mr. L.W.
After treatment.

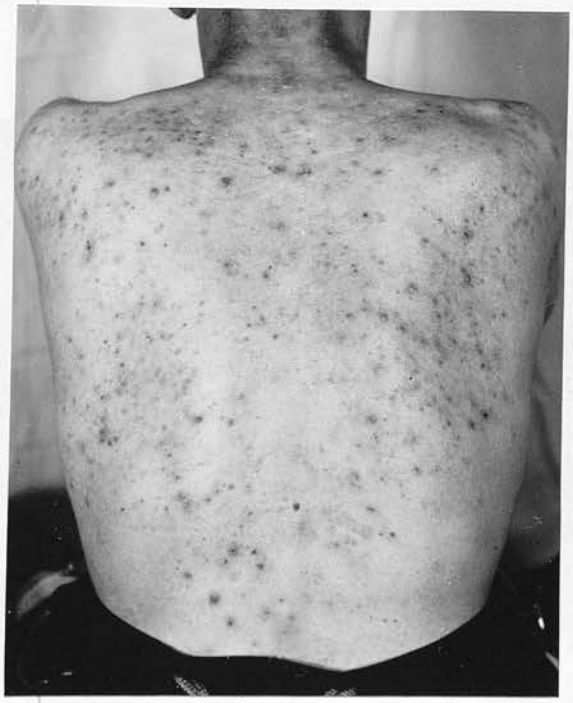


Fig. No. 54C. Mr. J.T.
Before treatment of Acne Vulgaris
with blackheads.

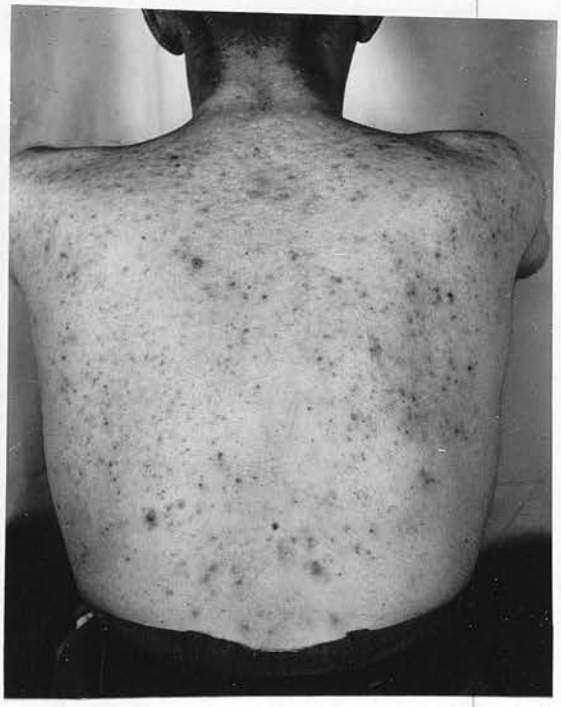


Fig. No. 54D. Mr. J.T.
After treatment.

Fig. No. 55A. Miss A. McG.
Before treatment of Acne Vulgaris.

Fig. No. 55B. Miss A. McG.
After treatment.

Fig. No. 56A. Mr. J.I.
Before treatment of Acne (cystictype).

Fig. No. 56B. Mr. J.I.
After treatment.

Fig. No. 57A. Miss J.F.
Before treatment of Acne Vulgaris.

Fig. No. 57B. Miss J.F.
After treatment.

Fig. No. 58A. Miss I. McD.
Before treatment of Acne Vulgaris.

Fig. No. 58B. Miss I. McD.
After treatment.

Fig. No. 59A. Miss J.H.
Before treatment of Acne Vulgaris.

Fig. No. 59B. Miss J.H.
After treatment.

Fig. No. 60A. Miss M.P.
Before treatment of Acne
Vulgaris with blackheads.

Fig. No. 60B. Miss M.P.
After treatment.

No.	Name	Sex	Age	Lesions	Months of Vit.A	Remarks
1	(contd.)					appeared after holidays which got well with vit. rich food. No recurrence in 8 months
2	C.G.	F	19	Papulo-pustules on face and back	3	Cleared in 2 months. No relapse in 9 months
3	C.N.	F	14	Oily face & papules on face	3½	Cleared in 3 months. No recurrence.
4	A.W.	M	21	Oily face & papulo-pustules on face & back & chest	3½	Cleared away completely. No recurrence
5	N.McD.	M	16	Do.	3	Do.
6	J.McC.	M	15	Do.	3½	Do.
7	K.D.	F	21	Papules on face & brittle nails	3	Cleared away and nails also became normal. No recurrence
8	J.T.	M	23	Do.	3	Do.
9	J.I.	M	18	Papulo-postules on back	5	Do.
10	C.W.	M	16	Greasy face and comedones	3½	Do.
11	W.M.	M	18	Do.	4	Do.
12	M.McA.	F	20	Oily face and papules on chest and chin	2	Do.
13	J.M.	M	15	Do.	2½	Do.
14	S.M.	M	16	Oily face & comedone on face, chest and back	4	Do.

(cont.) From page 133.

No.	Name	Sex	Age	Lesions	Months of Vit.A	Remarks
15	J.C.	M	23	Papulo-postules on face	3½	Cleared but re-curred & further 2 weeks treatment cleared
16	A.H.	M	18	Oily face and papules	2½	Cleared completely
17	J.S.	M	18	Cystic type on face and back	5	Completely cleared away except one on neck which had to be aspirated
18	J.Y.	M	18	Oily face and papules on face and neck	3	Completely cleared away
19	J.I.	M	19	Do.	2½	Do.
19A	S.L.	F	35	Blackheads on back and face with papules on face and back	4½	Cleared away. No relapse
20	I.McD.	F	15	Do.	3¾	Do.
21	P.G.	F	22	Oily face and blackheads with few papules on face	4¼	Cleared away but relapsed after 6 months
22	E.K.	M	17	Papulo-pustules type on face	3¼	Cured. No relapse
23	W.C.	M	20	Do.	2½	Do.
24	E.B.	F	22	Papules and come-dones on face and back	2½	Do.
25	S.S.	M	24	Papulo-pustules on face	3	Do.
26	J.M.	M	38	Com - pap back and face	3	Do.
27	W.F.	F	19	Papules on face	2	Do.

No.	Name	Sex	Age	Lesions	Months of Vit.A	Remarks
28	R.R.	M	18	Pap-pus. on face and back	3	Cured. No relapse
29	I.P.	F	28	Comedone on back and face	4	Completely cleared. No relapse
30	C.C.	F	17	Com- pap and oily-ness	4½	Do.
31	A.McP.	F	20	Comedone on face, neck and back	4	Do.
32	T.B.	F	23	Do.	4	Do.
33	J.H.	F	16	Do.	4½	Do.
34	M.L.	F	18	Oiliness of face and comedone	4	Do.
35	H.T.B.	M	21	Com - pap - pus	4½	Do.
36	G.Q.	M	25	Com - pus face	4	Do.
37	A.A.G.	F	15	Pap-pus face & neck	4	Cured in 2 months but relapsed. Controlled in 4 months
38	M.P.	F	22	Oiliness of face and papule	3	Cured. No relapse
39	E.T.	F	21	Pityriaris Cap. oily face & pap.	3½	Cured but no effect on Pity.Cap.
40	J.M.	F	17	Com - pap - pus face	4	Cured without relapse
41	J.F.	F	19	Pap-pus on face and back	3	Do.
42	A.S.	M	21	Com-papules on face and back	3	Do.
43	L.W.	M	15	Pap-pus on face	2½	Do.
44	E.Y.	F	21	Com - pap-pus face and neck	3½	Do.
45	J.R.	M	22	Pap-pus on back	3	Do.
46	M.M.	F	16	Pap-pus com on face	3	Do.

No.	Name	Sex	Age	Lesions	Months of Vit.A	Remarks
47	M.B.	F	23	Pap-pus & oiliness on face	3	Cured without relapse
48	J.C.	F	15	Pap-pus face	2½	Do.
49	T.M.	M	28	Com - pus face and neck	3½	Do.
50	M.B.	F	20	Com - pap-pus face & back	4	Do.
51	M.S.	F	23	Pap-pus on face	2½	Do.
52	N.O.	M	14	Com - pap-pus face and neck	3	Do.
53	J.T.	F	23	Oiliness and pup on face & back	2½	Do.
54	J.F.	F	19	Do.	3	Do.
55	J.M.	F	19	Do.	3	Do.
56	E.W.	F	16	Papulo-pus. acne on face & back	3¼	Do.
57	M.T.	M	22	Pityriasis Capitis with acne on face	3	Acne got cured but Pit.Cap. remained unaffected
58	G.L.	M	12	Pityriasis Cap. & papulopustular acne on face	3	Do.
59	J.F.	M	18	Papulo-pustular acne on face, back and chest	3	Cured without recurrence
60	R.N.	F	18	Papulo-pustular on face	3	Do.

Table No. XXXVII

Martial Status of Acne Patients

Total No. of Cases	No. of Males	No. of Females	Unmarried	Married
75	-	-	62	13
	39		33	6
	-	36	29	7

Table No. XXXVIII

Resistant cases of acne treated with oral administration of vitamin A in dose of 100,000 I.U. per day.

No.	Name	Sex	Age	Lesions	Months of Vit.A	Remarks
1	M.S.	F	26	Papulo-pustular on face and back	5	Completely cleared but recurred after 6 months
2	S.M.	F	12	Do.	4½	Cleared. No recurrence
3	C.E.	F	14	Oily face with papules	5	Oily face got well in 1½ months. Papules cleared in 5 months. No recurrence
4	W.Y.	M	21	Comedone on face and back with papules. Thick skin	5½	Papules cleared in 3 months & comedones took 5½ months
5	J.L.	M	19	Oily face and body with pustules and cysts. Thick skin	5½	Completely cleared. No recurrence
6	A.B.	M	21	Papules on face and brittle nail. Thick skin	3½	Cured with no recurrence
7	G.McD.	M	21	Cystic type on back and shoulder. Thick skin	4½	Do.
8	J.F.	M	18	Papulo-pustular on face, neck, shoulders. Thick skin	3½	Cured in 2 months but recurred, but with 3½ months treatment cured and no recurrence

No.	Name	Sex	Age	Lesions	Months of Vit.A	Remarks
9	L.W.	M	15	Papulo-pustular on face, neck, shoulders. Thick skin	4	Cured without recurrence
10	T.S.	M	16	Excessive pityriasis Capitis with oily face, body & limbs & papules on neck & shoulders. Thick skin	4½	Cured of acne and oiliness but pity. cap. did not improve
11	E.C.	M	20	Papulo-pustular with acne face. Thick skin	4	Cured but relapsed after 6 months
12	S.McL.	F	22	Comedones and papulo-pustules	4½	Cured without relapse
13	J.F.	M	18	Pityriasis capitis with oily face and papulo-pustules. Thick skin	3½	Cured but no effect on pity. cap.
14	E.McB.	F	26	Cystic acne on neck and back	5½	Cured but relapsed soon
15	C.W.	M	16	Cystic type. Thick skin	5½	Completely got well. No relapse

Table No. XXXIX

No. of cases requiring periods of treatment with Vit.A.

Total No.	No. of Cases	Length of time in months	Result
75		2 - 4 months	Cured 60. Improved 15
	40	3	All cured except 5 cases
	20	3½	All except 6 cases
	10	2	All except 1 case
	5	4	2 only cured

BESNIER'S PRURIGO : 16 cases have been investigated. Blood vitamin A and carotene values are normal. Two of these cases were treated with vitamin A in dose of 100,000 I.U per day for a month and then the dose was doubled per day for 3 months more without any effect (Table No. XIX page 96).

NEURO DERMATITIS : 7 cases have been investigated. Both the vitamin A values and carotene value are normal. 2 of these cases were treated with vitamin A in dose of 100,000 I.U. daily per month for 3 months without any remission either clinically or aymptomatically (Table No. XX - page 98).

ALOPECIA : 7 cases have been investigated. One of the cases was a case of Pseudo pelade de Brocq and the other 6 were cases of alopecia ariata. Vitamin A and carotene values showed normal figures. 4 cases including ten case of Pseudo pelade de Brocqu were treated for 3 months by oral administration of vitamin A in dose of 100,000 I.U. daily with no improvement except one case of alopeora areata showed some improvement (Table No. XXl - page 99).

HIGHER VITAMIN A NUTRITION.

LUPIS ERYTHEMATOSUS : 6 cases of chronic discord type of cases have been investigated for

vitamin A nutrition. Higher Vitamin A and lower carotene levels have been observed. No trial with vitamin A therapy was tried (Table No. XXll - Page 100).

The values for androgen excretion in urine is very low in cases of lupns erythermatosis. The values range between 1.31 to 3.3 of 17 keto steroids in in the 2 disseminated types and in the chronic discoid type the values are just below the normal values (Table No XXXL - page 118).

KERATODERMA PALMARIS ET PLANTARIS :

Only 2 cases of congenital type have been investigated. Vitamin A values show higher than normal (Table No. XXIII - page 118). Since these cases showed higher vitamin A nutrition vitamin A restriction advised but no change in the clinical condition could be observed evern after 4 months. Later on vitamin A in dose of 100,000 I.U.orally was started and both the patients showed slight improvement in the form of smoothness but not thinning of the Keratosis of palm and sole when treatment was continued for 3 months.

LICHEN PLANUS : 15 cases have been investigated Both vitamin A and carotene values in the blood values showed much higher values than normal (Table No. XXXI- page 118). Advice of a vitamin A restricted diet for 3 months could not produce any improvement. The urinary androgen values were normal (Table No. XXIV- page 118).

PSORIASIS : 17 cases have been investigated. Blood vitamin A values showed higher values but carotene value was normal - Table XXV - page 102). Vitamin A restricted diet in 8 cases showed but slight improvement in 2 cases. Urinary androgen excretion was found within normal range. Table No. XXV - Page 102).

D I S C U S S I O N.

Far-reaching advances have been made in the field of nutrition during the past two decades. More and more diseases are being associated with dietary deficiences, especially with inadequate supplies of certain vitamins.

The science of vitaminology is, as yet, a relatively young one, but in quite a short time a vast and rapidly expanding literature embracing the field of dermatology has been produced. It must not be assumed, however, that the research, entailing such an adventurous conquest of new territories, has pursued an untrammelled course. The road to discovery has been beset by many pitfalls. Attractive hypothesis have been advanced, too hastily accepted and as hastily rejected. Too frequently the wide gap existing between the laboratory experiment and the clinical trial on the human has not been appreciated sufficiently and speculation and ill-formed concepts have held sway for limited periods among evidence which is never static but continually grows and fluctuates.

RELATIONSHIP OF NUTRITIONAL DEFICIENCY TO METABOLIC DISTURBANCES OF THE SKIN.

The idea that certain dermatological conditions are due to a general or cellular disturbance of

carbohydrate or fat matabolism is a rather old one. It has been in disfavour with the dermatologists because of the disappointing results obtained in the early days of blood chemistry and basal metabolism tests. For example, the much-favoured carbohydrate diet for acne vulgaris and other skin diseases based on a 'seborrhoic disturbance' has received a severe blow by the findings of normal blood sugar values and sugar tolerance curves in such patients. The danger of excessive carbohydrate intake lies in the well-established lack of vitamins in sugar and refined flour. To make matters worse, an increase of carbohydrate intake in the diet increases the demand for vitamins.

DEFICIENCY OF VITAMIN A.

Human vitamin A deficiences can be recognised by (1) Clinical examination, (2) measuring dark adaption and (3) estimating vitamin A in blood.

In the present investigation blood vitamin A estimation has been done and vitamin A clearance tests in a limited number of cases for the assessment of vitamin A nutrition and also to ascertain the vitamin A utilisation of the subject.

METHOD FOR VITAMIN A ESTIMATION : The method for vitamin A estimation is that of Carr-Price(1936). Recently a method for estimation of vitamin A in the

blood has been reported by Sobell and Snow(1947).

After trying both the methods it has been found that lower values of blood vitamin A is found by Carr-Price method and the colour which develops and is measured by the spectro photometer for the amount of vitamin A is very transitory making the accurate reading difficult. Saponification of the serum gives a higher vitamin A value by Carr-Price method. Saponification for 20 minutes has been advocated by some workers (Bessy et al, 1946) but on saponifying for different lengths of time highest vitamin A value has been found when saponified for 60 minutes. While in the G.D.H.method of Sobell and Snow(1947) there is no change in vitamin A values after saponification and gives even higher values without saponification when compared to the values by Carr-Price after 60 minutes saponification.

Hence in the present investigation a modified method of Sobell and Snow(1947) has been followed by using unsaponified serum.

In the present work investigation of the vitamin A nutrition has been carried out on 114 normal human subjects comprising both males and remales and the average values for vitamin A being 171 international unit and for carotene being 69 international unit.

Separately for males and for females the values are :

for 56 males vitamin A being 200 I.U. and carotene being 64 I.U.

for 58 females vitamin A being 142 I.U. and carotene being 73 I.U.

Males show higher vitamin A values whereas females show higher carotene values.

The results of the present investigation in 114 normal human subjects are quite consistent with results of some of the workers (Table No.XXXVI - page 140).

Table No. XXXVI.

Comparison of vitamin A nutrition of different workers.

No.	Name of Worker.	Year.	Country.	Vit.A.in I.U. per 100 cc blood	Carotene in I.U. per 100 cc blood
1	Author	1949-50	Scotland	171	69
2	Campbell & Tonks	1949	Wales	108	80
3	Medical Research Council, London.	1949	England	128	100
4	Leitner & Moore	1946	England	113	Nil
5	Yudkin	1941	England	113	120
6	With	1940	European Continent	40-100	20-50
7	Lindquivest	1938	-do-	110-400	Nil
8	Schneider & Widmann	1935	-do-	240-450	30-80
9	Menken	1934	-do-	250	Nil

No.	Name of Worker.	Year.	Country.	Vit.A.in I.U. per 100 cc. blood.	Carotene in I.U. per 100 cc blood.
10	Kagan	1950	U.S.A	126	Nil
11	Hoffmann	1947	-do-	43	146
12	Wright & Niedelman	1947	-do-	90	36
13	Sobel & Snow	1947	-do-	46	22
14	Bessey	1946	-do-	50	141
15	Booher	1945	-do-	100 to 300	50 to 300
16	Haig & Patek	1942	-do-	108	80
17	Kimble	1939	-do-	109	176

Since in the United Kingdom different values for liver vitamin A storage has been found for different places it is consequently possible to have different blood vitamin A values for different places although the food is more or less the same all over U.K. due to its being controlled by the Ministry of Food with the balanced food under rationing system.

Liver concentration of vitamin A for England being 300 units per 100 gram of the liver (Harris and Moore,1947) and in Scotland 500 units per 100 gram (Dzialoszynski and Tomaszewsji,1947). This low liver vitamin A in England is quite consistent with the low blood vitamin A of 128 I.U. as compared with 171 I.U. blood vitamin A in Scotland where the vitamin A concentration of the liver is 500 units (Table No. XXXVII - page 142).

Table No. XXXVII.

Comparison of liver and blood vitamin A values of England with that of Scotland.

Place	Vit.A.in I.U. in liver per 100 gram.	Vit.A.in I.A. in blood per 100 cc.
England	300	128
Scotland	500	171

VITAMIN A CLEARANCE TEST.

This test is of value to find out the utilisation of vitamin A in the body which causes the latent deficiency of vitamin A in the system. Vitamin A clearance test is done by administering vitamin A by mouth immediately after collecting venous blood and then the blood is collected every 2 hours 6 times and again 24 hours and 32 hours after administration of vitamin A. Ruch(1946) has studied the vitamin A clearance test and has found in normal human subjects the maximum concentration in vlood at the sixth hour after oral vitamin A falling to the initial value in 24 hours. In the present investigation vitamin A clearance has been found to be differemt when vitamin A in 100,000 I.U. administered orally and intramuscularly. In the normal subjects the values returned to the initial values at the end of 24 to 32 hours (Fig.Nos. 9 and 12 - pages 110).

INFLUENCE OF VITAMIN A ON SKIN.

Some believe that the first property to be established of vitamin A was its ability to stimulate growth. Subsequent studies by different workers

revealed other functions of vitamin A such as the normal acuity of vision, and to help in maintaining normal body coverings and linings.:

VITAMIN A AND SKIN CHANGES

EXPERIMENTAL DERMATOLOGY : A nutritional approach to experimental dermatology should beging with a thorough study in experimental animals of the skin diseases which can be produced by nutritional means. The experience on laboratory animals has to be utilized in the clinical trial on dermatological patients.

IN ANIMALS.

With the development of the science of nutrition there have appeared numerous contributions on the changes in the skin of various animals fed on deficient or abnormal diet. Among the numerous nutritional investigations have been reported in recent years there may be found many descriptions of skin changes which occur in animals fed on experimental diets.

Localized and generalized alopecia, 'denuding' alteration in the texture and the colour of the hair, erytherma, edema, scaling, dermatitis, ulcerations, crust formation, purpura and atrophy associated with other signs of malnutrition have been observed in animals on vitamin deficient diets in the laboratory. In many cases skin changes may be indications of the general poor condition of the animal which has been subjected to an abnormal diet. However, Sullivan and Nicholls(1940) have found, that certain deficiency states in animals are constantly accompanied by

definite skin abnormalities and the assumption seems warranted that specific nutritional factors are essential for normal skin metabolism. McCollum and his co-workers(1939)have revealed various changes in skin and mucous membrane in rats on vitamin A deficient diet. Sullivan and Nicholls(1940)have also observed that lesions appeared when the animals were 4 weeks of age than when they were older and are in the form of scabby ears and tails, sores on the nose, sore feet and ragged hair. Atrophy of hair folliclies and sebacious glands followed by Kratinizing metaplasia with obstruction of the gland ducts have been observed in rats, guinea pigs, dogs and monkeys with vitamin A deficiency (Wolbach and Howe,1925 and 1926). Loss of subcutaneous fat with reduction of total number of hair follicles observed in rats on vitamin A deficient diet (Portman,1927). Under strict experimental conditions with a diet containing decreased amount of vitamin A, Moult(1943) could produce in rats progressive skin changes with Keratinized and follicular hyperkertosis with distended plugs in the hair follicles Kertinizing metaplasia of the epithelium is the most important change observed in animals due to airtaminosis A. McCullong and Dalldorf(1937) have experimentally proved in rats that the formation of Kratimized epithelium may result from deficiency of vitamin A. Hyperkratosis of the pilosebaceous follicles in rats with vitamin A deficiency has been experimentally produced by Moult(1943).

IN HUMAN SUBJECTS.

Sufficient experimental evidences have been collected to indicate that the results obtained in experimental animals have a widefield of application in human pathology.

The recent researches in vitamins have given a stimulus among the Dermatologists in co-operation with the Biochemists to correlate the knowledge of nutrition with certain skin changes.

The characteristic lesions of the skin and mucous membranes in nicotinic acid deficiency in itself signifies that cutaneous eruption can develop as a result of cellular disturbances which have their origin in nutrition. Biochemists have recognized that cellular disturbances are due to an interference with the process of biologic oxidation and other enzymatic functions, which fits in well with the concepts first expressed by the founder of modern histopathology of the skin, P.G.Unna.

The morphological differences in the dermal manipulations resulting from deficiences of vitamin A, nicotine acid, riboflavin and vitamin C offer a pattern for the study of other cutaneous disorders which may be caused by malnutrition.

The rapid developments of recent years in the field of vitamins had had their influence on dermatological thinking. In 1925 Wolbach and Howe showed that vitamin A deficiency produces histological changes in the epithelical tissues. They described these changes as follows: in the early stages of

vitamin A deficiency, areas of darkly stained epithelial cells are seen to undergo rapid growth. As they grow the underlying epithelium degenerates and is sloughed off. Islands of stratified, squamous and Keratinized patches form. When this condition is treated with adequate vitamin A the process is reversed. First there is a separation of the Keratinized layer and vacuoling of the cells of the intermediate layer. The upper zone deteriorates. The Keratinized cells are then pushed off and their places taken by the deep zone cells which are normal and not keratinized.

Skin metaplasia is the most important of all the different forms of metaplasia due to dietary deficiency of vitamin A.

Skin lesions due to vitamin A deficiency were first reported by Nicholls(1931)in India and Frazier and Hu(1931)in China.

CUTANEOUS MANIFESTATIONS OF VITAMIN A DEFICIENCY

Cutaneous manifestations of vitamin A deficiency had long been known to the dermatologists(Brocq,1890 Duhring,1886;Crocker 1905) under the descriptive terms as Keratosis Rilaris,lichen pilaris,lichen spinulosus and so on.

Cutaneous manifestations due to deficiency of vitamin A in man were first studied systematically by Pillat(1929). Later on Frazier and Hu(1931) and Reiss(1936) studied the condition in China.,Lowenthal (1933) in Africa,Nicholls(1933)in Ceylon,Aykroyd and Rajagopal(1936) and Rao(1937)in India and Fasal(1944)

in Malaya. Youmans and Corlette(1938) and Lehman and Rapaport(1940) reported the first cases in U.S.A.

Frazier and his associates (1943) observed the specific pathological changes in the skin resulting from vitamin A deficiency and think that skin lesions are directly due to epithelial metaplasia. Normal epithelium becomes keratinized. In the early stages dryness and roughness of the skin are the only signs. These are caused by hyperkratosis and parakratosis of the epidermis and by hypofunction of the sebaceous and sweat glands due to hyperkratinization of the lining epithelium of these glands, which ultimately results in their atrophy. In fact vitamin A deficiency leads to an atrophic stage which is characterized by thinning of the epidermis. When dryness is mild, it is often more readily detected by palpation than inspection.

The next stage resembles an exaggerated state of goose flesh. The more advanced cases are characterized by hyperkratotic follicular lesions appearing at the sites of the pilosebacious follicles,principally on the anterolateral aspects of the thighs and the posterolateral aspects of the upper arms and forearms. The eruptions may then spread to the shoulders, back, buttocks, abdomen and in some cases, to the face and posterior aspect of the neck as well. Hands and feet are never involved. These eruptions vary from filiform processes to small, conical papules with a central plug which projects from the surface or is covered with a loosily process which projects from the

surface or is covered with loosely adherent scale or contains a broken-off or coiled,unerupted hair. When the follicular keratosis are pronounced,they give the skin a rough,greater-like feel,whence the name nutmeg grater skin given by Stabbus(1941).

The author has observed in India during the 12 years of his dermatological practice, and particularly after the Bengal famine of 1943 and after the partition of India in 1947, various cutaneous manifestations due to deficiency of vitamin A (Lahiri,1945) Lahiri,1948 and Lahiri,1949).

VITAMIN A AND DIFFERENT SKIN DISEASES

Different skin diseases for which vitamin A is supposed to be responsible may be discussed under different groups such as (1) skin diseases associated with hypovitaminosis A, (2) skin diseases associated eith hypervitaminosis A and (3) skin diseases due to defect in utilisation of vitamin A.

SKIN DISEASES ASSOCIATED WITH HYPOVITAMINOSIS A.

Only three different skins conditions such as Ichthyosis,Pityriasis rubra pilaris and Nummular Eczema could be investigated in the present work.

ICHTHYOSIS.

Increase of the normal skin markings is a feature of the earliest cutaneous change in avitaminosis A. Fasal(1944) has observed an increase of skin markings in the early stages of vitamin A deficiency and he has observed ichthyosis in markedly vitamin A deficient cases. Stannus(1944(is of

opinion that this condition is a disturbance which maybe partly tranmatic in origin and partly due to deficiency of vitamins A, B and E. The essential factors other than vitamin A may be concerned is supported by the experimental findings in animals by Sullivan and Evans(1945). Rappaport and his associates(1942)suggest that vitamin A deficiency might be an etiological factor in ichthyosis and they attribute the condition of ichthyosis to an hereditary disturbance of vitamin A metabolism. Low blood vitamin A level has been found in ichthyosis by Mashkieleison and his co-workers(1945). Leitner and Moore(1946) have also found low vitamin A in the blood in cases of ichthyosis. Cornbleet and Popper (1942) have experimentally found that vitamin A is absent from the epidermis even after large doses of vitamin A administration in cases of ichthyosis. Kaposi (quoted by Ormsby and Montgomery, 1948) states that the cause of ichthyosis appears to be a local anomaly of the nutrition of the skin.

Blood vitamin A estimation has been done in 7 cases in the present investigation (Table No.XXII - page 92) and the vitamin A nutrition has been found to be below normal in all the cases. All the cases have been treated with oral vitamin A therapy in dose of 100,000 I.U.daily. Improvement started after a month and the skin started feeling soft and smooth with the disappearance of the feeling of dryness,

roughness and peeling within 6 weeks on an average in 5 cases but only in 2 cases 4½ and 5 months treatment was necessary. Patients were treated for 3 months on an average and followed without treatment for nine months more without relapse.

THERAPEUTIC EFFECT OF VITAMIN A IN ICHTHYOSIS.

Kingery(1926) found changes in the thyroid and suprarenals at necropsy in a case of ichthyosis which suggested an endocrine disturbance as an etiological factor. While investigating basal metabolism in ichthyosis Porter(1926) observed a subnormal basal metabolism rate in 70 per cent of children and 25 per cent adults. Thyroid has been used with benefit by many dermatologists in this skin disease. Peck and his co-workers (1943) have observed low vitamin A in blood and with administration of vitamin A have been able to raise the blood vitamin A with improvement in the skin condition. The author has found very encouraging results in ichthyosis with vitamin A (Lahiri,1945). The administration of vitamin A in ichthyosis has been advocated by Ormsby and Montgomery (1948).

Cases of ichthyosis improve with thyroid because thyroid helps the conversion of provitamin A to vitamin A and this vitamin A corrects the epithelium of the alimentary cannal which helps absorption and conversion of greater amount of provitimin A and vitamin A and cures the disease.

PITYRIASIS RUBRA PILARIS.

Pityriasis rubra pilaris is a very rare disease particularly where the diet is balanced as in U.K. This disease is characterized by hard, yellowish or reddish papules which are situated at the mouths of the hair follocles and oil gland ducts and which may become generally or even universally distributed (Sutton and Sutton Jr.1939). In addition there is often palmer and planter kratoderma, as well as seborrhoic dermatitis (Urbach and Le Winn,1946). The etiology of this disease which runs an intractable course was entirely unknown until quite recently, when Pettler(1936) first demonstrated that great improvement could be achieved by giving large doses of Vitamin A. This relationship was clarified largely by the important work of Brunsting and Sheard(1941) who in each of three cases demonstrated impaired dark adaption which returned to normal threshold levels during the course of appropriate vitamin A treatment with 150,000 units daily. Vitamin A therapy continued for months, resulted in a slow and definite, but not complete improvement of the skin.

THERAPEUTIC EFFECT OF VITAMIN A.

O'Leary and his associates (1944) have reported great benefit with vitamin A therapy in a child with pityriasis rubra pilaris and they have further observed that on three occasions the vitamin A therapy was stopped for a month, with arecurrence each time of the waxy palms and soles and just as regularly,

there was disappearance of the lesions after resumption of the therapy. A number of the authorities including Peck and Chargin(1941), Ebert(1942), Weiner and Levin(1943) and Ormsby(1944) have reported similar results. Thomas(1946) has treated with success a case with 200,000 units of vitamin A daily in 4 months, Fox(1944) treated a case of pityriasis rubra pilaris with a daily dose of 200,000 units of vitamin A by mouth.

In U.K. Leitner and Moore(1946) reported the relationship of vitamin A with pityriasis rubra pilaris and they have also found consistently low values of carotinoids and vitamin A in the blood of patients. Leitner and Ford(1947) believe that pityriasis rubra pilaris is probably always an inherited condition. This may be latent and precipitated by malnutrition and patients improve quickly after administration of vitamin A and severe cases need prolonged treatment with vitamin A.

The author has treated only 4 cases of pityriasis rubra pilaris in India and had the opportunity to follow only 2 cases up to the end of 1948 that is for an average period of 16 months.With 100,000 I.U. dose of vitamin A for 6 months only cleared the skin conditions except the keratosis of palms and soles. There was no relapse in these two cases for ten months without vitamin A (Lahiri,1950). The author found low blood vitamin C and quicker therapeutic response in a case in 1946 of pityriasis rubra pilaris when treated with a combination of vitamins A, C and E (Lahiri,1949).

Out of the two cases, the author had the opportunity to see in Edinburgh under Professor Percival during 1949-50, one died of coronary disease and the other case got cured with vitamin A Therapy for a period of 7 months.

In contradistinction to the authors mentioned above Gross(1941) is of the opinion that, because of the response to niacin, yeast and liver therapy, pityriasis rubra pilaris is caused by a complex deficiency rather than vitamin A alone. He submits the hypothesis that vitamins A and B complex deficiency is the cause of this skin disease.

O'Leary(1943) believes that there are pathologically two types of pityriasis rubra pilaris. The patients who are improved by vitamin A Therapy and demonstrably afflicted with night blindness. In the other group, composed of individuals with normal dark adaptation, he assumes the presence of a complex deficiency similar to that postulated by Gross.

Vitamin A Therapy in high dose has been found to be of immense value and is also advocated by many in the routine Therapy of pityriasis rubra pilaris. Brunsting and Sherd(1941) have advocated intramuscular injection of 20,000 units of vitamin A. 2 to 3 times daily for 2 months. In the case investigated in the present work no response was observed with daily injection of vitamin A for 2 weeks.

Pettler(1936) was the first to treat two cases of pityriasis rubra pilaris with vitamins. Later he treated a boy with carotene only and the patient improved in one month and there was no relapse within 4 years (Pettler,1942). Arguello(1940) treated a woman with 20,000 I.U. of vitamin A for 3 months successfully. Sobell and Pollock(1948) successfully treated one case with vitamin A. Brunsting and Sheard(1941) treated 3 cases with a daily dose of 150,000 I.U. of vitamin A successfully for 3 months. Peck and Chargin(1941) have successfully treated one case with 200,000 I.U. vitamin A daily for 2 months. Prosser Thomas(1943) has not found good results in 9 months in a patient whom he treated with vitamin A in dose of only 12,000 I.U. daily. Forman(1943) did not see any improvement with vitamin A injection. Fox(1945) treated successfully a woman who had an extensive relapse of pityriasis rubra pilaris after more than 30 years. Except for some scaling on the scalp, the eruption completely disappeared with 200,000 I.U. of vitamin A for a year. Weiner and Levin(1943) investigated a family suffering from pityriasis rubra pilaris where the blood vitamin A and carotene levels were within normal limits but ingestion of carotene caused temporary improvement and 100,000 to 200,000 I.U. of vitamin A daily gave rise to definite improvement in all cases within 4 weeks and 90 per cent skin lesions disappeared in 3 to 6 months time.

Cessation of vitamin A administration was followed by relapse within 4 weeks.

The only case of pityriasis rubra pilaris investigated in the present work showed a low vitamin A but did not show any clinical improvement during the 2 weeks the patient was given 100,000 I.U.vitamin A by intramuscular injection.. Two weeks after the oral therapy with vitamin A in the same dose clinical improvement could be seen and thereafter improvement in the clinical condition became marked with raising of blood vitamin A level as shown by monthly investigation of blood vitamin A (Fig.No.10 page 126).

The urinary androgen estimated in this case at the beginning and on repeating at the end of active therapy with vitamin A showed lowering of the androgen figure to one third.

This high androgen certainly disturbed the normal estrogen-androgen ration in the system. Whether this hormonal imbalance is responsible for destruction of vitamin A in the liver or helps the formation of vitamin antagonists is difficult to understand. But with the lowering of androgen level with vitamin A therapy the estrogen-androgen inbalance possibly gets corrected and with the correction of estrogen metabolism the destruction of vitamin A in the liver seems to end. In an established case there seems to be some deficiency in the absorption of provitamin A and vitamin A from the alimentary tract and

with the institution of vitamin A therapy the epituclinum of the intestinalget back to its normal physiological condition. This helps in absorption of provitamin A and vitamin A from the alimentary tract and increases the conversion of provitamin A to vitamin A in the intistinal wall and the result is shown by the rise in the blood vitamin A level. Ultimately proper vitamin A nutrition either spares estrogen which brings down the high androgen or spares vitamin E which untilately corrects in some way the estrogen-androgen imbalance in the system and helps the proper metabolism and utilisation of vitamin A in the system.

NUMMULAR ECZEMA.

An increase demand for vitamin A in the functions of the integument by exposure to cold, steam heat, alkaline and water and scratching could be incriminated for eliciting visible manifestations of an otherwise latent deficiency of vitamin A. The distribution of nummular eczema further suggests location with a high demand on adequate function of sebacious glands. Gross(1941) found beneficial result in nummular eczema with vitamin A therapy and postulates a hypothesis that an increased initability of the epidermal nerve endings due to an alteration of the epithelium caused by vitamin A deficiency. Peterkin (1949) has also found beneficial effect with vitamin A in cases of nummular eczema.

The author has treated cases of nummular eczema in India with vitamin A orally combined with local treatment with very encouraging results. (Lahiri,1948).

In the present work 7 cases of nummular eczema have been investigated as regards vitamin A nutrition. Blood vitamin A levels have been found to be low in all the cases (Table No.XVIII, - page 94). On an average period of 4 months all the cases responded to oral therapy with vitamin A in dose of 100,000 I.U. daily except in one case who was suffering from pulmonary tuberculosis also.

MISCELLANEOUS SKIN DISEASES ATTRIBUTED TO HYPOVITAMINOSIS A

Besides the three different types of skin diseases due to deficiency of vitamin A have been investigated in the present work there are a large number of skin diseases for which vitamin A nutrition has been held responsible in some way or other.

Baer and Vogel(1940) and Wise and Subzberger(1938) have cured dryness of the skin, mild ichthyosis, keratosis; pilaris, brittleness of the nail and dryness and brittleness of the hair with vitamin A therapy. In the present investigation also brittleness of the nail associated with some cases of acne vulgaris got completely cured with vitamin A therapy.

Pseudopelade like lesions of the scalp have been observed in vitamin A deficiency by Goodman (1941). Other workers like Wise and Sulzberger (1938) have also noted similar results in lichen spinulosus with folliculitis decalvans. Garfield (1942) has used vitamin A therapy successfully in 2 cases of lichen spinulosus. In the present investigation of a case of pseudo pilade de Brocq has been investigated. The blood vitamin A did not show avitaminosis A and 3 months vitamin A therapy could not produce any improvement in the case.

The similarity of the histology of the lesions in Keratosis blennorhagica with those of keratosis follicularius due to airtaininosis A led Combes and Behrman (1942) to study the effect of vitamin A therapy on the skin eruption. There was a striking improvement in the skin lesions of their patient after other forms of therapy had failed. This raised the question whether Keratosis blenonorhagica might not occur in paticuls into gonoorhorea who had in addition some disturbance of the vitamin A metabolism.

Straumfjord(1940) has preseted observation suggesting that vernix caseosa may be a manifestation of vitamin A deficiency in the newborn. He questions whether vernix caseosa is a normal substance because many normal babies are born with none.

Experimentally giving vitamin A to pregnant women he has observed the role of vitamin A in the causation of vernix caseosa in the newborn babies.

Porokeratosis Mibelli has been treated by the author in India with high doses vitamin A for a prolonged period with success in one case (Lahiri,1948) and Ghose(1948) treated successfully some case of porokeratosis Mebilli with vitamin A therapy in the skin department of the Calcutta School of Tropical Medicine (India).

Congenital Keratosis of the skin of palm and sole (Mal de Meleda) has been found to be associated with ichthyotic skin. Brunner and Fuhrman(1950) have observed improvement with 300,000 I.U. of vitamin A daily in a case of Mal de Meleda. Author has treated 3 cases of congenital Keratosis of palms in Indian children with success by liver diet and liver extract therapy and he thinks that the improvement was due to vitamin A in the liver (Lahiri,1948)

Whittle(1950) has recently found low vitamin A nutrition in colloid milium and thinks that the colour of the lesions is reminiscent of tylosis, a condition in which vitamin A metabolism is disturbed, with low plasma vitamin A. Cohen(1949) believes that the peculiar colour of colloid milium is due to carotenoids which is the provitamin A. It is possible that the changes of colloid milium are bound up with a local disturbance of vitamin A metabolism in the skin.

Pigmentation of the Skin : changes in the colour of the skin in vitamin A deficiency has been observed by various workers. The normal colour of the skin fades and becomes shallow and ashen grey, in children and adults alike, and the change in the colour becomes more and more pronounced the longer the vitamin A deficiency lasts. It shows first on the face, which may assume an appearance similar to that of chloasma uterinum subsequently, the extensor aspects of the forearms and legs, as well as the chest become affected (Pillat, 1939). In some cases, the skin in general has a dull, slaty colour. Tolmach and Graham(1942) have observed a case presenting innumerable prifollicular deposits of pigment. After ten weeks of treatment with high doses of vitamin A, pigmentation had been reduced about 50 per cent. Lowenthal(1935) reports that the skin of the Uganda natives changes from a lustrous to a dull grayish black, especially on the extensors or sides of the extremities, on the hips and in the gluteal zone. The alteration in the colour of the skin is attributable, first to the fact that the epithelium becomes less and less transparent as the disease continues, with the result that the blood vessels of the corium cannot give the skin its normal pinkish colour. This is due to the multiplication of the cellular layers in the epethelium, and at the same time, the

progressive dehydration of the epithelial cells and the accelerated cornification (Pillat,1939). Another reason for the change in the colour of the skin is the increase in pigmentation (Urbach and Le Winn,1946). By means of Bloch's dopa reaction, Mu and his co-workers (1937)succeeded in demonstrating the presence of abnormally great amounts of melanin in the skin of individuals suffering from vitamin A deficiency.

Benedek(1947) found pigmentation of skin of the trunk, face and limbs in soldiers returning home to U.S.A. from Japan and he attributed the cause to deficiency of vitamin A in the food.

The author has reported 7 cases of macular bluish pigmentation of skin (melanosis) in adult vegeteranians in India who were cured with parantral liver therapy for a period of 10 weeks. The patients complained of itching of the skin and presented bluish prifollicular macular pigmentation of the neck, exposed part of the chest, hand and legs. Cases showed high eosinophilia in the blood and pathologically showed increase of pigmentation in the basal layer and also in other layers of the epidermis with hyperkeratosis (Lahiri,1948). The author also treated another group of 5 cases after the Bengal famine in adults with similar picture and three patients responded easily to high vitamin A orally in dose of 300,000 I.U. daily for only 3 weeks

(Lahiri,1949). The author concluded from his experience in treating these new clinical entities in India during 1943 to 1948 that vitamin A seems to be responsible for controlling the pigment metabolism of the skin. Proper vitamin A nutrition keeps the excessive pigment formation in check.

DARIER'S DISEASE : Peck and his associates (1941) claimed for the first time that Darier's disease is due to vitamin A deficiency. Peck and his co-workers (1943) believe that dyskeratosis follicularis is a disease of vitamin A deficiency due either to hereditary or an acquired weakness in the absorption of vitamin A or in the conversion of provitamin A into vitamin A. But Leitner(1946) disagrees with this view as he has established with certainty that the absorption of vitamin A was not interfered with in his cases and believes that there is no conclusive evidence as yet whether the conversion of carotene into vitamin A or the utilisation of vitamin A is affected.

Low plasma vitamin A has been found in Darier's disease (Leither and Moore, 1946), Mashkieleison and his associates (1945) have also observed low blood vitamin A concentration in Darier's disease. In the investigation of 5 cases Leitner (1946) observed low level of blood vitamin A and Moore (1946) also found very low blood vitamin A values in all 3 of his cases of Darier's disease. Thomson(1946) also noted

low blood vitamin in one case of Darier's disease.

VITAMIN A THERAPY : Leitner(1946) treated with success 3 cases of Darier's disease with vitamin A in dose of 120,000 I.U. per day. In treating 9 cases of Darier's disease with vitamin A in dose of 200,000 units, Peck and his associates(1947) observed complete cure of the condition.

The only case the author has seen of Darier's disease in this country was a case demonstrated in Edinburgh on the 15th July 1950 on the occasion of the annual meeting of the British Association of Dermatology and Syphilis. The case was getting vitamin A in high dose for over a month but so far no marked improvement could be noticed. The author has not seen any case of Darier's disease in India although cutaneous diseases due to avitaminosis A are very common in India.

PHRYNODERMA : The skin changes which occur as a result of deficiency of vitamin A was described by Nicholls(1933) in India who first used the name toad skin or phrynoderma, and Lowenthal(1933) in the same year in Africa, who made his observations without knowing that the importance of vitamin A for the skin had already been recognized two years before in China by Frazier and Hu(1931). In England a few cases were reported in children by Goodwin(1934) and by Pemberton (1940) while May and Wolff(1938) noticed changes in the skin and nails of an infant with xerophthalmia. In America Lehman and Rapaport (1940) reported nine cases in children and reviewed the literature. Pallister

(1940) found toad skin common in Malaya.

There is, however, still some uncertainty as to whether toad skin is due to simple deficiency of vitamin A or whether some other factors are also involved. In favour of a deficiency of vitamin A being the only cause is the work of Lowenthal(1938), who cured two of his cases with vitamin A alone,and practically all the rest with codliver oil, while Lehman and Rapaport(1940) cured their cases with halibut-liver oil. Pallister(1940) in Malaya noted an association between toad skin and Bitots spots. Steffens and others(1939) produced typical changes in the skin of a man by a vitamin A deficient diet. Nicholls(1934) and Lowenthal(1935) have noted a close association between skin changes and night blindness or xeorphthalmia, this association being apparently far commoner after than before adolesence. The author (Lahiri,1944) observed association of phrynodermia with xsophthalmia amongst children referred from the eye department to his department of skin diseases in a teaching hospital in India. In a series of 272 cases during 1943 to 1945 after the Bengal famine routine codliver oil treatment cured 97 per cent of the cases in an average period of 4 months and the rest 3 per cent cases took about 6 months when together with codliver oil injections of liver extract were given biweekly for 2 months. The author concluded that phrynoderma is due only to vitamin A deficiency in children and adolescent boys and girls when there is a great demand of vitamin A

for general growth and particularly bones and endocrine glands function(Lahiri,1945).

Against these observations, however, must be put those of Aykroyd and Rajagopal(1936-37) and Rao (1938) who did not find any close correlation between toad skin and xerophthalmia, or between the former and a diet deficient in vitamin A during a very extensive investigation of Indian school children. Frazier and Hu(1931) and Sweet and K'Ang(1935) found no correlation of the skin and eyes, so that they decided that in children the eyes but not the skin were affected by a deficiency of vitamin A; while after adolescence they chiefly suffered. This is confirmed by Frazier and his associates(1943) who showed that in young children the skin is generally only xerotic and atrophic follicular hyperkeratosis seldom occuring before adolescence. The problem is still further complicated by the descriptions given by Fox(1941) and Wiltshire(1919) of the early skin changes in scurvy which appear to be almost identical with those of toad skin.

The position appears to be that lack of vitamin A alone can cause toad skin, but that there is often some other factor which alters the reaction of the skin so that it is more sensitive to a deficiency of vitamin A. This ancillary factor may be either a second food deficiency (Rao,1938), or the stage of sexual development (Frazier et al,1943), or a

familial need for abnormally large amounts of vitamin A (Goodwin,1934; Cornbleet,1938; Aykroyd and Rajagophal,1936) or a racial susceptibility such as is apparently shown in India (Nicholls,1933; Aykroyd and Rajagophal,1937) and in Africa (Lowenthal,1935) but not in China (Frazier and Hu, 1936; Sweet and K'Aug, 1935). Others state that it may ultimately cover the whole body apart from the face, which is seldom involved (Nicholls,1933; Rao, 1936-37) although "black-heads" are common (Frazier et al, 1943; Sweet and K'Aug,1935). The scalp is not affected, but the hair may be dry and brittle and the nails have transverse or longitudinal ridges (Sweet and K'Aug,1935), though generally the hair and nails are normal (Frazier and Hu.1933; Nicholls,1933) while others have not found it (Rao, 1938) including the author in a series of 272 cases in India (Lahiri,1944).

The eruption of phrynoderma consists of dry horny round or oval sharply defined papules, varying in diameter from that of a pin's head to as much as a split pea (Lowenthal,1933; Lahiri,1944). The size of the papules increases with the duration of the deficiency, in the early stages more easily felt by the fingers than seen, while later the skin looks from a distance as if many split lentils had been stuck upon it. Each papule is formed by hyperkeratosis of the pilosebacious follicles and has a hard

keratinous core which can be picked out, leaving a small pit. Often broken or coiled up unerupted hairs are found either projecting through the papule or imprisoned beneath. The papules seldom, if ever, undergo pustulation (Sweet and K'Aug,1935; Lahiri, 1944).

Whatever the cause the reaction of the skin varies so much that sometimes changes occur before there is obvious involvement of the eye (Frazier and Hu,1936; Pemberton,1940, Herrin,1940; Aykroyd and Rajagopal,1936-37) or even slight impairement of dark adaptation (Steffens et al,1939), while in other cases the eyes may be seriously damaged while the skin apparently remains normal.

The insidious onset of a dry rough skin especially in those areas where the papular eruption occurs later, is the first cutaneous symptom of a deficiency of vitamin A. Such skins are not uncommon in children attending out-patient departments of hospitals,though they are often missed, frank toad skin being rare at this age. Goodwin(1934), Lowenthal(1933) and Frazier and Hu(1936) all stress this early symptom, which has been noted at all ages from infancy to old age and in both sexes. There is an increase in the spring after the deficient winter diet (Sweet and K'Aug,1935; Breese and McCoord,1939). The dry skin may be followed by a sudden local eruption which often spreads rapidly over the fronts and sides of the thighs, and

the posterior and lateral sides of the forearms just below the elbows, and the fronts of the arms and shoulders. Some observers report that the eruption generally spares the front of the chest (Nicholls, 1935), the groins and axillae, and the backs of the hands and feet (Frazier and Hu.1935; Frazier et al,1943; Lowenthal,1933; Nicholls 1934; Lahiri,1944 and Rao,1938) though Young(1941) believes that the skin is more susceptible to fungus infection. It has also been observed by the author that fungus infection takes a very long time to clear in patients with phrynoderma and when fungicides are locally applied together with oral cod liver oil or vitimin A therapy the fungus takes a surprisingly short time to cure (Lahiri 1945).

VITAMIN A THERAPY : The treatment with vitamin A is entirely successful of the cases of phrynoderma. The first sign of recovery is a return of sweating so that the skin within two or three weeks no longer feels dry (Frazier et al, 1943; Lehman and Rapaport 1940), though it does not return to normal for 2 to 9 months, the s horter period being on very high doses of vitamin A such as 100,000 international units per day. Concentrated preparations or even injections have been advocated (Sweet & K'Aug,1935) The Keratotic plugs in the follicles are reported to be extruded as tiny-rice-like bodies, but by remaining partly adherent to the skin they give to

it a shaggy appearance (Lehman and Rapaport,1940). Ultimately the epidermis and the follicles return to normal and new hairs develop (Bicknell and Prescott 1948). The author has observed complete cure of the lesions with codliver oil by mouth and weekly injections of liver extract and high protein diet in 4 to 6 months time (Lahiri,1945). Recently the author has found oral vitamin A in dose of 100,000 international unit to be helpful in curing the condition in an average period of 4½ months (Lahiri, 1948).

SKIN DISEASES ASSOCIATED WITH HYPERVITAMINOSIS-A

In the four following types of skin diseases investigations have been carried on for vitamin A nutrition:

LUPUS ERYTHEMATOSUS : This condition has been found to be affected by pregnancy and also by hyperthyroidism. Both in pregnancy and in hyperthynoidism there is increased conversion of carotene above normal due to overaction of the thyroid (Drill and Mathices,1946). In the present work 6 cases have been investigated. Blood vitamin A is higher than normal but the carotene is very low (Table Nos.XXII page 100). 17- Ketosteroids in 24 hours urine has also been estimated. The androgen excretion in urine has been found to be low in 6 cases of discoid chronic lupus erythematosus and much lower in 2 cases of subacute disseminated lupus erythematosus (Table Nos.XXXI and XXII - pages 117 & 110).

KERATODERMA PALMARISET PLANTARIS : Only two congenital cases have been investigated. Although blood vitamin A values are higher (Table No.XXIII page 100) than normal vitamin A therapy in dose of 100,000 I.U. per day for 3 months almost cleared away keratosis of palm and sole. It is very difficult to explain this effect, but it is possible that probably utilisation of vitamin A is defective although blood shows higher level of vitamin A. Recently Porter and Haber (1950) have reported beneficial effect with vitamin A therapy in a case of acquired keratosis Palmaris et Planteris.

LICHEN PLANUS : 15 cases have been investigated in the present work. Both the blood vitamin A and carotene show higher levels than normal (Table XXIV - page 101). Like psoriasis the defect in Lichen planus cases may be an inherent one in the utilisation of vitamin A or a greater conversion of provitamin A to vitamin A giving rise to changes in the skin. It is not known whether endocrine function plays any part in it.

PSORIASIS : Since keratoplasia has been observed in vitamin A deficiency by a host of workers (Wolbach and Bessey,1942; Wolbach and Howe; Youmans and Cornbleet,,1938) and a defect in the reactive process of Keratinization appears appears to be an essential factor in the histopathology of psoriasis.

It is quite likely that the improvement of psoriasis subsequent to the Grutz-Burger low-fat diet might be due to the simultaneous decrease in the supply of vitamin A.

Vitamin A nutrition has been found to be abnormally high in 17 cases of psoriasis investigated in the present work (Table No. XXV-page 102).

Urinary androgen has been found to be normal (Table No. XXXI-page 117).

SKIN DISEASES DUE TO DEFECT IN THE UTITSATION OF VITAMIN A

In the following 4 different types of skin conditions probably the utilisation of vitamin A is defective due to heredity or due to some endoesine abnormality. In 3 types of cases such as Besnier's Prurigo, Neurodermatitis and in Alopecia areata blood vitamin A levels have been found to be normal. Vitamin A was tried orally in dose of 100,000 I.U. in 20 cases of Besnier's Prurigo, in 7 cases of neurodermatitis and in 7 cases of alopecia for a period of 4 to 6 months without any effect. Probably vitamin A plays no part in the causation of these three varieties of skin diseases.

ACNE VULGARIS : This is one of the 4 different kinds of skin diseases where deficient vitamin A utilisation has been supposed to be the cause of the condition.

Acne Vulgaris has been fully investigated from the point of view of the utilisation of vitamin A.

Various factors supposed to play their role in the patho genesis of acne. They are : (1) heredity (Stokes and King,1932), puberty (Bloch, 1931), endocrine disturbances (Cohen,1941), seborrhoea (Jacquet and Rondean,1905), infection (Yap,1937), diet and digestive disturbances (Whitfield,1934), disturbances in water balance (Stokes et al,1938), exoginous substances such as iodine (Sulzberger et al,1934), bromide (Vedroff, 1928), coal tar derivatives (Butler,1937) and oils (Schwartz,1941). Acne has been attributed to deficiency or excess of most of the hormones (Cohen,1941) although the hormone imbalance cannot be described to any known or detectable cause. Klaude and Mackie(1940) have made diet and digestive disturbances responsible. (Sutton(1941) has emphasized the role of excess fat intake and has also observed in fat restricted diet. A study of the fat tolerance as indicated by blood cholestrol changes following the ingestion of fat, failed to reveal any difference in tolerance in patients with and without acne vulgaris (Le Winn and Fingerman, 1942). Anderson and Williams (1937) have observed that the infants at breast receive about half the calories in the shape of fat and acne is rare in them. Butterworth(1941) did not find acne amongst Eskimos whose diet is essentially fat with high vitamin A daily. The acne associated with hypothyroidism cannot be reasonably attributed to antagonism between vitamin A and Thyroxin for no actual

inhibition of Thyroxin by vitamin A could be demonstrated experimentally by Baumann and Moore(1939).

ENDOCRINE : Acne Vulgaris occurs only during the period of activity of the ovaries and testes and hence the importance of the endocrine factors in the causation of acne is emphasized. Hamilton (1941) while treating 31 prepubertal boys who were cryptorchids, ennuchoids and adult castrates with injections of testosterone propionate observed the influence of androgen on sebacious activity and the formation of comedones and of the papules and pustules of acne. He observed that abnormally high quantities of androgen is not required for the development of acne but the presence of an effective concentration of body tissues and fluid is needed. Barber(1948) has observed that in both sexes acne normally results only from androgenic stimulation of the follicles, whereas estrogens have the opposite effect. It has been further observed by Lawrence and Werthessen(1949) that acne is caused by a disturbance of the normal balance between androgen and estrogen and they have also assumed that such an imbalance may be due to in certain persons to a deficiency and to others to an excess. It has been experimentally and clinically observed in a long series of acne cases both in men and women that patients with acne vulgaris showed a lowered estrogenic output than the control group and it has been concluded that the adolescent type of acne is a

sex hormone imbalance (Wile,1939). Wile found out the ratio of the andrógenic and estrogenic output in acne patients which were quite different from the control group. The spontaneous cure of acne following the completion of adolescence and the entrance into the marital status would seem to indicate the restoration of the normal ratio between estrogen and androgen (Wile,1939). Many dermatologists believe that acne vulgaris is due to a prepondance of androgenic hormone over estrogenic hormone and the treatment along these lines has proved very successful (Belisario,1950).

The importance of thyroid hypofunction in the causation of acne has been found by many. Vilanova and Canadell(1949) have made some interesting observations to show that the skin of 2 juveniles with long-standing hypothyroidism showed follicular hypekeratosis in addition to signs of myxaedema.

VITAMIN A : Where there is a deficiency of Vitamin A there is noted follicular hyperkeratosis frequently at the time of puberty (Frazier et al, 1943). There are two factors in the causation of acne vulgaris namely, the first is the patients' endocrine status and the second being the utilization of vitamin A and thus Keddie(1948) thinks that the skin altered by endocrine imbalance is peculiarly susceptible and may demand large amounts of vitamin A for normal function.

BURROWS(1945) has observed that estrogen effects on the skin and vaginal mucous are similar to the changes seen in Vitamin A deficiency. Keddie(1948) observes that the circulating estrogen may act on the epithelium either by direct antagonism between estrogen and vitamin A in the skin or vaginal mucosa. Since there is an antagonism between estrogen and androgen, estrogen may influence indirectly the formation of acne vulgaris.

It seems significant that in true vitamin A deficiency, as well as in acne vulgaris, the maximal degree of sexual development appears to be the critical factor in the response of the pilosebaceous structures of a deficiency of vitamin A (Obermayer,1948). Keddie(1948) has experimentally shown that the administration of estrogen produces an accentuation of the need of the skin for vitamin A.

In the present work 75 cases of acne vulgaris have been investigated (Table No.XV - page 87).

Blood Vitamin A on an average has been found to be normal (Table No. XV - page 87), although some of the cases shown low blood vitamin A levels. By the vitamin A clearance tests it has been found possible to show in cases of acne vulgaris that there is defect in vitamin A utilisation and this could be said latent deficiency of vitamin A (Table Nos. XXVII and XXIX - pages 105 & 109).

Vitamin A clearance tests in 6 cases of acne vulgaris when compared with clearance tests in 6 normal human subjects (Fig. No. 12 - Page 110), show a much lower blood concentration at the sixth hour after administration of oral vitamin A in cases of acne vulgaris. Vitamin A clearance test is improved with the improvement of the skin diseases with vitamin A condition therapy (Fig. No.16 - page 111).

Estimation of urinary androgen shows higher values in acne vulgaris before vitamin A therapy and lowering of the androgen values after 3 months vitamin A therapy and cure (Table No. XXXII - page 118). A comparison of vitamin A in blood and urinary androgen estimations before and during the course of vitamin A therapy show that improvement starts with the lowering of the androgen excretion in the urine and simultaneous increase of blood vitamin A (Fig. Nos. 14 and 15 - pages 132 & 118B). This confirms the inter relationship between the maintenance of the balance of androgen and estrogen with proper vitamin A nutrition. (Fig. No. 15 & 118).

Statistically compared with cases the blood vitamin A and carotene mean deviation is not of much significance. Hence low blood vitamin A cannot be said to be the cause of vitamin A deficiency directly but the vitamin A clearance tests show significant results both before and after treatment (Fig. No. 16 - page 111).

This shows that there is defect in utilisation of vitamin A inthe body in patients of acne vulgaris and this gives rise to the imbalance of estrogen and androgen in the acne patients.

RELATIONSHIP OF BLOOD VITAMIN A TO CERTAIN SKIN DISEASES

HYPOVITAMINOSIS-A : Although vitamin A has great influence on the skin physiology skin contains vitamin A in no appreciable amount has been shown by Cornbleet and Popper (1942). All the epidermal parts are affected by indirect means through the metabolism of vitamin A (Cornbleet et al,1944). How this is brought about is difficult to understand but it seems likely that the liver under the influence of hormones brings about cutaneous vitamin A metabolish. Vitamin A metabolish is affected in various skin diseases such as xeroderma, ichthyosis, pityriasis rubra pilaris, phrynoderma, Darier's disease whereas vitamin A values in the blood is increased in lupus erythematosus, keratosis palmaris et plantaris, lichen planus and psoriasis.

The influence of gonadal hormones on the morphological changes wrought by vitamin A on the skin has also been observed by Frazier and his associates (1943). In children vitamin A deficiency causes phrynoderma, ichthyosis and pityriasis rubra pilaris but during adolescence when there is greater

pilosebaceous activity vitamin A deficiency causes acne. Recently it has been shown by Booth(1950) by experiment that the sex hormones has an influence on the storage of vitamin A in the body. It has been found also that in some of the skin diseases, particularly in acne vulgaris there is an imbalance of the estrogen and androgen hormone. Since vitamin A has been found to clinically improve acne and simultaneously lowers the androgen excretion it is likely that in this state when androgen hormone is much in excess in the urine it either acts directly or by destroying Vitamin E lessens the antioxidant or by helping in formation of vitaminantagonist which brings about the destruction. As it has been found that vitamin A storage in the liver is increased if vitamin E be administered at the same time (Hickman and Harris, 1946). This vicious circle which starts during pubertal age due to a greater demand for vitamin A, for other tissues of the body and particularly for bone development, may sometimes persist even into the young adult age unless treated with vitamin A to correct the condition. Overproduction of androgen in the body causes acne vulgaris has been proved by many workers. Acne vulgaris of the face, chest and shoulders is seen to appear in the presence of tumours that lead to the overproduction of androgen in the body (Shelly,1950). It has been experimentally proved by animal experiment that androgen acts

as an antagonist to the changes produced by estrogen (Zahler,1950).

Evidence has been found in the present investigation to show that vitamin A influences some dermatological conditions. Although in acne vulgaris vitamin A level in blood shows normal values but vitamin clearance test shows deficiency in utilisation of vitamin A in the system which is corrected when acne vulgaris is cured with vitamin A therapy. The androgen excretion in acne vulgaris which is initially high is brought down to normal (For male 15 mg and for female 8 mg are normal values) with Vitamin A therapy and consequent cure of the condition.

In cases of pityriasis rubra pilaris androgen was very high which gradually came down with simultaneous rise of blood vitamin A level resulting in amelioration of the symptom with vitamin A therapy. Here also gonadal hormone seem to influence the skin condition.

In cases of ichthyosis no definite high androgen values have been found but with the administration of vitamin A skin conditions improved almost like normal skin and there has not been a relapse of the condition for a long time after stopping vitamin A therapy. It is quite likely that in ichthyosis the endocrine gland responsible is the thyroid because thyroid administration also improves the condition. This improvement is brought about by helping the conversion of provitamin A to vitamin A. Low blood vitamin A level

in hypothyroidism and with administration of thyroid extract clearing of the signs of avitaminosis A has been experimentally observed in patients by Vilanova and Canadell (1949). Vitamin A therapy in ichthyosis probably corrects the associated latent hypothysoidism which helps in converting the provitamin A to vitamin A and thus ultimately helps in the proper absorption of vitamin A and provitamin A from the intestine and conversion of provitamin A to vitamin A. In ichthyosis of the younger age group thyroid is the only hormone seems to be responsible in its causation whereas in the older age group vitamin A deficiency probably also upsets the estrogen-androgen balance.

The same is true for other skin conditions where hypo-vitaminosis A is associated.

HYPERVITAMINOSIS-A : Cases of hypervitaminosis have been reported in children (Josephs,1944), in an adult (Toomy and Morissette,1947) and another case in an adult by Rothman and Leon(1948). The symptoms of hypervitaminosis A are characterized by elevated vitamin A levels in the blood and anorexia, loss of weight, irritability low grade five, pruriginous rash, sparseness of hair, hepatomegaly and tenderness of bones (Fried and Grand,1950). Fried and Grand believe that since storage of vitamin A and regulation of its blood levels are functions of the liver the symptoms and signs in hypervitaminosis develop due to the hepatic dysfunction rather than the super saturation of the liver with the vitamin.

Knowledge concerning etilogy and pathology of psoriasis, lichen planus, keratoderma palmaris et plantaris and lupus erythematosus is limited. The most important function of the epidermis is to produce Keratine for the skin. In the skin of a psoriatic the mechanism of Keratinization fails. Instead of completely Keratinized cells, defectively cornified are produced (Samberger,1921). The extent and degree of parakeratosis are related to the clinical activity of the disease. Quiescent and healing lesions show hyperkeratosis in place of parakeratosis (Haslund, 1912). Since a defect in the reactive process of Keratinization appear to be an essential factor in the histo-pathology of psoriasis and since keratoplasia is observed in vitamin A deficiency (Wolbach and Bessey,1942), it is quite likely that the improvement with low-fat diet of Grutz-Burger in psoriasis might be due to the limited supply of vitamin A. In the present investigation vitamin A nutrition has been found high in cases of psoriasis. Hoffmann and his co-workers(1947) have also observed higher vitamin A nutrition in psoriatics.

A low-fat diet has been recognized in the treatment of psoriasis (Grutz and Burger,1933) because they thought that psoriasis is a "Lipoidosis" and that a lowering of the fat content of the cutaneous elements was the basis of the beneficial effect.

Le Winn and Zugerman(1941) have experimentally found increased lipids in the blood as in the skin of psoriotics. Psoriatic lesions markedly improved or completely cured within a certain period of time after institution of a diet restricted in both provitamin A and vitamin A (Hoffmann et al,1947). Androgen excretion in the present investigation has not been found abnormal in cases of psoriasis,lichen planus, keratosis palmaris et plantaris and in lupus erythematosus but it is quite likely that the controlling influence on blood vitamin A has been put out of gear.

It has been found experimentally that human subjects saturated with vitamin A did not develop signs of vitamin A deficiency even after a period of six months on a diet limited to low vitamin A (Wald et al,1942). On a restricted diet blood provitamin A level falls extremely low at the end of a week (Brenner and Roberts,1943) and this has also been confirmed by Hoffmann and his associates(1947) in cases of psoriasis.

Von Euber (1932) thinks that the conversion of carotene tovitamin A probably occurs in other tissues besides liver and that the carotene may have biologic function in addition to being the precursor and main source of vitamin A (Zechmeister,1934 and 1937). Hoffmann and his co-workers(1947) emphasize the possibility that the carotene itself has a direct

influence on skin matabolism must be considered. Whether or not stimulation of keratinization due to vitamin A restriction is the basis for the observed improvement in psoriatics with restricted vitamin A diet is difficult to understand. But the endocrine factor seems to be responsible in bringing about the proper metabolism and utilisation of vitamin A in the system.

S U M M A R Y

1. Vitamin A nutrition assayed by estimating vitamin A in blood.

2. The Carr-Price method of vitamin A estimation is compared with the G.D.H.method. Saponification of serum is necessary for Carr-Price method of estimation. Maximum vitamin A value is obtained by Carr-Price method only when serum is saponified for 60 minutes. G.D.H.method with unsaponified serum gives comparable values.

3. Vitamin A clarance test is helpful to find out utilisation deficiency of vitamin A.

4. Urinary androgen estimations have been done in some of the skin patients. In some of the patients low blood vitamin A and high urinary androgen have been found.

5. Result of vitamin A therapy in high dosage for a period of 3 months on an average is found to be beneficial in some of the skin cases.

6. As a result of vitamin A therapy some of the cases of skin diseases showed lowering of the androgen levels with simultaneous raising of the vitamin A levels. Even in some of the resistant cases of acne vulgaris, with the lowering of the urinary androgen and raising of the blood vitamin A values with

vitamin A therapy, definite clinical improvement in the skin condition has been observed.

7. In 114 normal human subjects the vitamin A nutrition values are : (a) average vitamin A being 187 Int.Unit for 100 cc of blood, (b) Aberage provitamin A being 68 Int.Unit per 100 cc of blood,

and separately for different sexes are :

(a) Average of 56 normal males vitamin A being 200 Int.Unit per 100 cc of blood

(b) Average of 56 normal males provitamin A being 65 Int.Unit per 100 cc of blood

(c) Average of 58 normal females vitamin A being 174 Int.Unit per 100 cc of blood

(d) Average of 58 normal females provitamin A being 71 Int.Unit per 100 cc of blood.

8. Vitamin A nutrition in 170 cases of skin diseases are as follows :

No.	Name of Disease.	No.of case investigated.	Blood Vit.A in I.U per 100 cc blood	Provitamin A in I.U. per 100 cc blood.
1.	Ichthyosis	9	131	73
2.	Pityriasis rubra pilaris	1	84.5	25
3.	Nummular Eczema	15	115.6	59
4.	Besnier's Prurigo	16	195.7	56
5.	Neurodermatitis	7	190	49
6.	Alopecia Areata	7	175.4	67
7.	Keratoderma Palmaris et Plantaris	2	212	65
8.	Lupus Erythema-tosus	6	210	38.7
9.	Lichen Planus	15	252.6	81.2
10.	Psoriasis	17	231.7	57.5
11.	Acne Vulgaris	75	175	59

9. Urinary androgen excretion in 24 hours urine has been estimated in 27 cases of skin diseases by the method followed in the Biochemical Laboratory, Royal Infirmary, Edinburgh.

10. Definite lowering of androgen excretion in urine with vitamin A Therapy has been observed in 6 cases of acne vulgaris and in 1 case of pityriasis rubra pilaris.

11. Vitamin A has been found to have great therapeutic value in skin cases showing low vitamin A nutrition such as Ichthyosis,

Pityriasis rubra pilaris and Nummular Eczema.

12. Some of the skin cases show higher vitamin A nutrition such as Lupus Erythematosus, Keratoderma palmaris et Plantaris with restricted vitamin A intake in diet.

13. Some skin cases show normal blood vitamin A levels such as Besnier's Prurigo, Neurodermatitis, alopecia areata and Acne vulgaris.

14. Cases showing normal vitamin A levels in blood show much abnormal vitamin A clearance tests.

15. Vitamin A therapy improves the vitamin A Clearance test. Improvement in clearance tests observed in clinically improved cases with vitamin A therapy.

16. Blood vitamin A level and urinary androgen level show definite relationship in cases of avitaminosis and also in cases showing abnormality in utilisation of vitamin A.

17. Vitamin A metabolism in the body seems to be controlled by endocrine functions. Gonadal and Thyroid secretions are mainly responsible for by it. It seems possible that vitamin A bringing down the androgen level maintains the estrogen androgen relationship in the body and thus brings about the cure of some of the skin diseases which are due to avitaminosis A and in

others helping the utilisation of vitamin A in the body. But in those showing hypervitaminosis A it is difficult to imagine if one single hormonal secretion or combined proper secretion of all the endocrine glands are responsible.

18. Vitamin A therapy alone is sufficient in some cases such as Ichthyosis. Pitriasis rubra pilaris and Acne vulgaris. In other cases such as in Nummular eczema vitamin A orally has also been found useful.

19. In cases of acne vulgaris it is essential to give trial with vitamin A therapy before instituting an irritating local peeling paste repeatedly or risky X-ray therapy and estrogen Therapy.

20. Vitamin A is a dependable and safe remedy for some of the skin ailments.

C O N C L U S I O N

All animals are able to synthesize vitamin A from yellow pigments, the carotenoids, found in plants. This synthesis takes place in the intestinal Wall and the vitamin A is mainly stored in the liver.

Vitamin A nutrition can be assayed accurately from the blood vitamin A and the utilisation of vitamin A of the subject is measured by the vitamin A clearance test.

Vitamin A has definite role in the causation of certain skin diseases. Some have shown hypovitaminosis A while others have shown hypervitaminosis A but in those where normal vitamin A nutrition has been found showed utilisation deficiency by clearance test.

Vitamin A therapy in dose of 100,000 international unit daily for a period of at least 3 months is useful in cases showing low vitamin A nutrition or defective utilisation capacity. Prolonged low vitamin A diet seems to be helpful in cases showing hypervitaminosis A.

Vitamin A seems to control the secretion of some of the endocrine glands to a great extent thus regulating the metabolism of skin. There is a definite interrelationship in the body between vitamin A nutrition and endocrine function.

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